DISSERTATION TITLED

"IMMUNE THROMBOCYTOPENIC PURPURA AND ITS ASSOCIATION WITH HELICOBACTER PYLORI INFECTION"

Submitted in partial fulfilment of

Requirements for

M.D.DEGREE EXAMINATION

BRANCH-I GENERAL MEDICINE

THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY

CHENNAI

INSTITUTE OF INTERNAL MEDICINE

MADRAS MEDICAL COLLEGE

CHENNAI - 600003.

APRIL-2013

CERTIFICATE

This is to certify that the dissertation entitled **"IMMUNE THROMBOCYTOPENIC PURPURA AND ITS ASSOCIATION WITH HELICOBACTER PYLORI INFECTION"**is a bonafide work done by **DR.ANNY ANTONY** , Post Graduate Student, Institute of General Medicine, Madras Medical College, Chennai-3, in partial fulfillment of the University Rules and Regulations for the award of MD Branch – I Internal Medicine, under our guidance and supervision, during the academic year 2010 - 2013.

Prof. N.RAGHU, M.D.,
Director & Professor
Institute of Internal Medicine,
MMC & RGGGH,
Chennai- 600003

Prof. K.S. CHENTHIL, M.D.,
Professor of Medicine,
Institute of Internal Medicine,
MMC &RGGGH,
Chennai-600003

Prof. V.KANAGASABAI, M.D.,
Dean,
Madras Medical College,
Rajiv Gandhi Government General Hospital,
Chennai – 60000

DECLARATION

I solemnly declare that the dissertation entitled "**IMMUNE THROMBOCYTOPENIC PURPURA AND ITS ASSOCIATION WITH HELICOBACTER PYLORI INFECTION**" is done by me at Madras Medical College, Chennai-3 during May 2012 to November 2012 under the guidance and supervision of Prof .K.S. CHENTHIL, M.D., to be submitted to The Tamilnadu Dr M.G.R Medical University towards the partial fulfillment of requirements for the award of M.D DEGREE IN GENERAL MEDICINE BRANCH-I.

Place: Chennai

Date:

Post Graduate: **Dr .ANNY ANTONY**
M.D. General Medicine,
Madras Medical College,
Rajiv Gandhi Government General Hospital
Chennai – 600003

ACKNOWLEDGEMENT

At the outset, I would like to thank **Prof.V.KANAGASABAI, M.D.,** Dean, Madras Medical College, for having permitted me to conduct the study and use the hospital resources in the study.

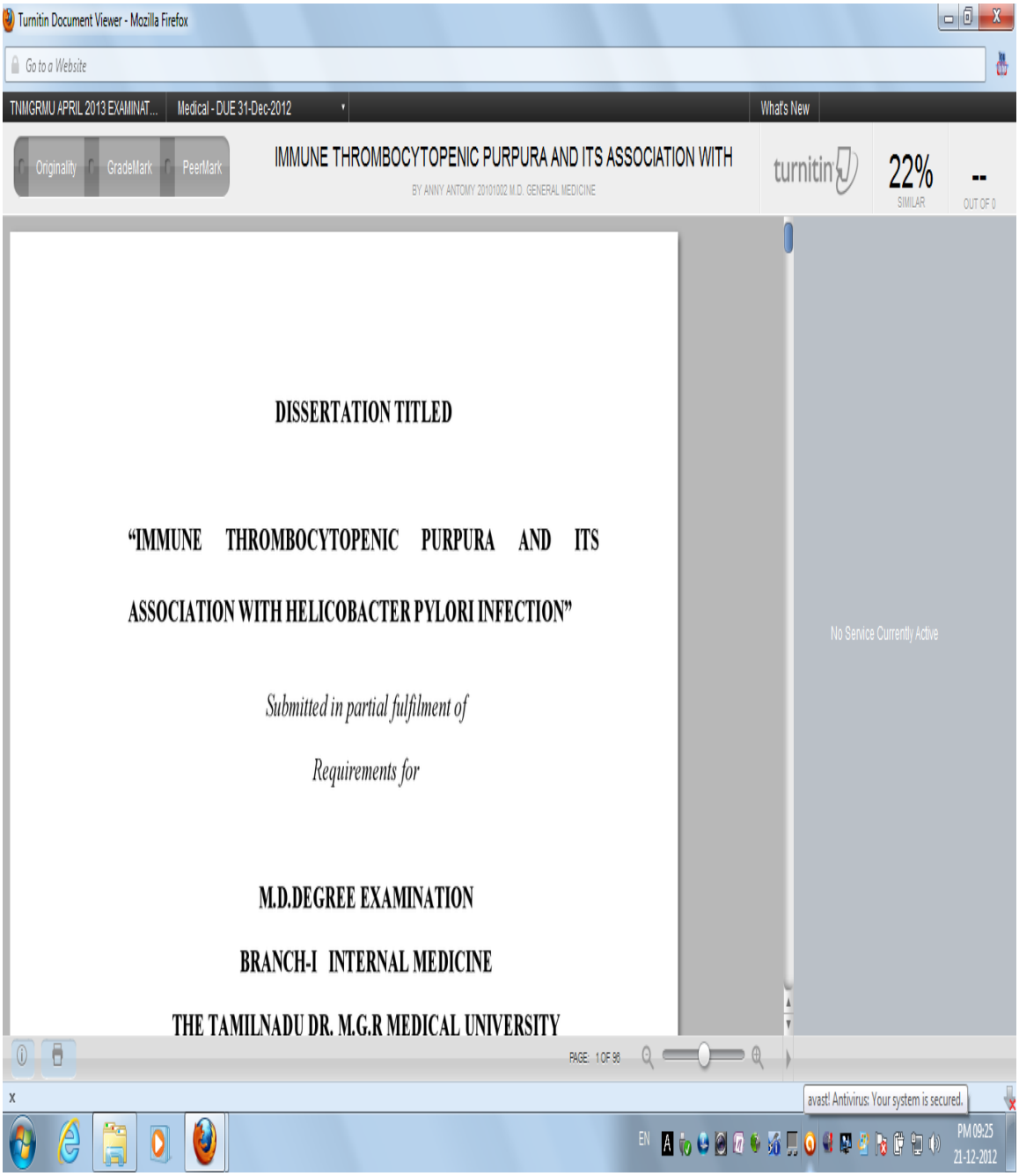
I express my heartfelt gratitude to **Prof N. RAGHU, M.D.,** Director, and Professor, Institute of Internal Medicine for his inspiration, advice and guidance in making this work complete.

I am indebted to my chief **Prof K.S. CHENTHIL, M.D.,** Professor, Institute of Internal Medicine for his guidance during this study. I am also extremely grateful to **Prof MARGARET.C, M.D.,D.M.,** Head and Professor, Department of Hematology and **Prof MOHAMMED ALI, M.D., D.M.,** Head and Professor ,Department of Medical Gasteroenterology, for their support and guidance.

I am extremely thankful to Assistant Professors of Medicine **Dr. S. BASKER, M.D., and Dr. ANUSUYA, M.D.,** for guiding me with their corrections and prompt help rendered whenever approached.

I thank the Professor, Assistant Professors and the technical staff in the Department of Hematology, Department of Medical Gasteroenterology

and Department of Biochemistry for their guidance and cooperation in the study. I am also indebted to thank all the patients and their caring relatives. Without their humble cooperation, this study would not have been possible.


Turnitin Document Viewer - Mozilla Firefox
Go to a Website
TNMGRMU APRIL 2013 EXAMINAT...
Medical - DUE 31-Dec-2012
What's New
Originality
GradeMark
PeerMark
IMMUNE THROMBOCYTOPENIC PURPURA AND ITS ASSOCIATION WITH
BY ANNY ANTOMY 20101002 M.D. GENERAL MEDICINE
turnitin
22%
SIMILAR
--
OUT OF 0
DISSERTATION TITLED
"IMMUNE THROMBOCYTOPENIC PURPURA AND ITS ASSOCIATION WITH HELICOBACTER PYLORI INFECTION"
Submitted in partial fulfilment of
Requirements for
M.D.DEGREE EXAMINATION
BRANCH-I INTERNAL MEDICINE
THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY
No Service Currently Active
PAGE: 1 OF 98
avast! Antivirus: Your system is secured.
PM 09:25
21-12-2012

CONTENTS

ABBREVIATION

ITP	Immune (Idiopathic) Thrombocytopenic Purpura
H.pylori	Helicobacter pylori
HIV	Human Immunodeficiency Virus
SLE	Systemic Lupus Erythematosus
TTP	Thrombotic Thrombocytopenic Purpura
HIT	Heparin Induced Thrombocytopenia.
WBC	White Blood Cell
TLC	Total Leucocyte Count
RBC	Red Blood Cell
DIC	Disseminated Intravascular Coagulation
MAHA	Microangiopathic Hemolytic Anemia
HCV	Hepatitis C Virus
LDH	Lactate Dehydrogenase

ESR	Erythrocyte Sedimentation Rate
CRP	C-Reactive Protein
PCR	Polymerase Chain Reaction
CMV	Cytomegalovirus
EBV	Epstein Barr Virus
MDS	Myelodysplastic syndrome
TRA	Thrombopoetin Receptor Agonists
GERD	Gastro esophageal Reflux Disease
PPI's	Proton Pump Inhibitors
RUT	Rapid Urease Test

INTRODUCTION

Immune thrombocytopenic purpura (ITP) also known as idiopathic thrombocytopenic purpura, is an acquired disease of adults and children which is immune mediated and is characterized by transient or persistent decrease of the platelet count. The risk of bleeding increases depending upon the degree of thrombocytopenia. When ITP occurs in the absence of an evident predisposing etiology it is known as primary ITP. and when it occurs secondary to an identifiable cause it is known as secondary ITP. Pseudo thrombocytopenia should also be ruled out.

Helicobacter pylori is an ubiquitous gram positive bacterium which was initially discovered in 1982. It colonizes the stomach of about half of the world's human population throughout their lifetimes. H.pylori has been clearly recognized as the main cause of gastritis and most cases of peptic ulcer .It also plays a role in the pathogenesis of gastric adenocarcinoma and mucosa associated lymphoid tissue (MALT) lymphoma It has also been implicated in the pathogenesis of some autoimmune diseases such as rheumatoid arthritis, autoimmune thyroid disease and ITP. Relevant to this Gasbarrini et al recently conducted a study and showed a high prevalence of H.pylori infection in patients with ITP and also reported a good response to bacterium eradication in most of the cases.

The relationship between H.pylori and ITP was initially described in 1998 in an Italian study. However discrepant reports have been produced by subsequent studies. In countries like Japan and Italy where the prevalence of H.pylori is high, the association between H.pylori and ITP was more frequent that is 70% and 50% respectively. Whereas in United States where the incidence of H.pylori is low the association was only 22%. Thus H.pylori prevalence in ITP patients mirrored the prevalence of H.pylori in the general population. However studies from France and Spain where the prevalence of H.pylori was high , did not show significant improvements in platelet count after eradication therapy.

Hence the association of H.pylori and ITP is still controversial. It is still not clear if H.pylori should be implicated as a secondary cause of ITP or it is just an alternative, additional or incidental finding in patients with ITP. All these possibilities have been suggested by different studies. In this study we aim to find the prevalence of H.pylori in ITP patients in our set up.

RESEARCH QUESTIONS:

1. Is there an association between H. pylori and chronic ITP?
2. Should patients with ITP be routinely screened and treated for H. pylori?
3. Does prevalence of H. pylori in ITP reflect prevalence of H. pylori in the general population?
4. Relation between H. pylori infection and age and H. pylori infection and dyspepsia symptoms?

AIMS AND OBJECTIVES

- To study the association between immune thrombocytopenic Purpura and Helicobacter pylori infection.
- To determine the prevalence of Helicobacter pylori infection in Indian patients with ITP.
- To evaluate if H. Pylori infected patients with ITP could be identified by symptoms referable to the GI tract.
- To study the clinical profile of ITP patients.

REVIEW OF LITERATURE

IMMUNE THROBOCYTOPENIC PURPURA

DEFINITION:

ITP is an acquired autoimmune syndrome in which antibody (which are directed against the platelet antigens) and cell mediated destruction of platelets and suppression of platelet production causes the platelet count to drop less than 1,00,000 cells/cubic mm and predisposes to bleeding depending upon the degree of thrombocytopenia.[2] It is a benign disorder. ITP in children is usually an acute and self limiting condition.

Phases of ITP [(3)]:

1. Newly diagnosed – diagnosis within 3 months of presentation.

2. Persistent ITP – thrombocytopenia lasts for > 3 months but resolves by 12 months. Includes patients who do not have spontaneous remission or patients who are not able to maintain complete response once they are off treatment.

3. Chronic ITP – thrombocytopenia lasts for > 12 months and requires continuous management.

4. Severe ITP: the patient presents with bleeding symptoms that mandates treatment or new bleeding symptoms occur which needs additional

therapeutic intervention in the form of increased dose of the drug or a platelet enhancing agent.

The bone marrow may show normal or increased megakaryocytosis in patients with persistent and chronic ITP. Bone marrow is usually done in patients > 60 years of age to rule out myelodysplasia.

ITP is a heterogeneous group of disorder in which there is autoimmune mediated destruction of platelet and impaired thrombopoiesis and this predisposes to bleeding.

INCIDENCE AND DEMOGRAPHICS[4]:

According to the UK health registry the incidence of adult onset ITP ranges from 1.6 to 3.9 per 1, 00,000 persons per year. The prevalence ranges from 9.5 to 23.6 per 1,00,000 persons. Initially adult onset ITP was believed to be a disease of young women, but recent studies have also shown an increased prevalence among older individuals. Males and females are equally affected in older age group whereas a female preponderance is seen among young adults.

ETIOLOGY[5]:

Based on etiology ITP is classified as given below:

1. Primary ITP: Occurs in the absence of a definitive predisposing etiology

2. Secondary ITP

The initial step in the evaluation of patients with ITP is to rule out the secondary causes of ITP.

Secondary causes of ITP:

1. Pseudo thrombocytopenia
2. Drug induced thrombocytopenia
3. HIV infection
4. Hepatitis C virus infection
5. SLE
6. Lymph proliferative disorders
7. Myelodysplasia
8. TTP
9. Congenital/hereditary thrombocytopenia
10. HIT (heparin induced thrombocytopenia and thrombosis)
11. H.pylori

In some patients H.pylori eradication corrects the thrombocytopenia and is considered as an alternative diagnosis. Whereas in some patients it is an additional disorder which worsens thrombocytopenia. In another group of patients it has no effect on the platelet counts and is considered as an incidental finding.[5]

Some rare causes of secondary ITP includes fetal and neonatal alloimmune thrombocytopenic purpura and post transfusion purpura.

PATHOGENESIS:

Life span of platelet is reduced due to antibody mediated lysis by tissue macrophages. There is suppression of megakaryopoeisis and megakaryocyte apoptosis. Lysis of platelet occurs due to direct peroxide injury. Immune mediated suppression of megakaryocyte and platelet development. T-cell mediated platelet destruction also occurs. There is also direct bone marrow suppression.

NON- AUTOIMMUNE CAUSES OF THROMBOCYTOPENIA IN ADULTS:[4]

1 Pseudo thrombocytopenia

2. Disorders of decreased platelet production: it includes viral infections, chemotherapy, radiotherapy, ethanol toxicity, congenital thrombocytopenia, folate or vitamin B12 deficiency, bone marrow disorders like MDS, myelofibrosis, and leukemia.

3. Disorders of decreased platelet survival: drugs like quinine and heparin, DIC, HUS, TTP, cardiopulmonary bypass, post transfusion purpura

4. Dilutional thrombocytopenia

5. Splenic sequestration: secondary to portal hypertension and infiltrative diseases of spleen.

DIAGNOSIS:

Primary ITP is a diagnosis of exclusion

HISTORY AND PHYSICAL EXAMINATION:

The clinical features are related to the platelet counts. Most of the patients present with mucocutaneous bleeding like bruising, gum bleeding, petechiae,

nose bleeds, heavy menses, hematuria, etc. Petechiae indicate a reduction of platelet number rather than a platelet dysfunction. Petechiae usually occur over areas of increased venous pressure so in ambulatory patients it is mainly seen over the ankles. Increased risk of life threatening hemorrhage in a thrombocytopenic patient is indicated by wet purpura that is blood blisters in buccal mucosa and retinal hemmorrhages.[1]

Symptoms pertaining to other diagnosis like antecedent viral infection, weight loss, fatigue, rash, joint swelling, lymph node enlargement, headache , personal history of autoimmune diseases etc. Family history of bleeding disorders (hemophilia, von Willibrand's disease), autoimmune diseases, immunodeficiencies or bone marrow failure syndromes should be ruled out. Assess abdomen for hepatomegaly and splenomegaly and mental status changes to rule out intracranial bleed. Look for ecchymosis and unequal pupils. Examine the testicles for males as thrombocytopenia may be the presenting symptom of leukemia.

LABORATORY EVALUATION:

Complete blood count, reticulocyte count

Peripheral smear study

Quantitative immunoglobulin (IgG, IgM, IgA)

Bone marrow examination (in selected patients especially when leukemia or myelodysplasia is considered)

Blood grouping and typing (to administer immunoglobulin)

Direct Coomb's test (if patient has concurrent anemia)

HIV, HCV

LDH, uric acid, ESR, CRP

Glycoprotein specific antibodies and antiphospholipid antibodies

Anti-thyroid antibodies and thyroid function

Antinuclear antibody

Serum protein electrophoresis

PCR for parvo virus, CMV, EBV.

Stool antigen test or urea breath test for H. pylori in high prevalent areas

Tests of unproven benefit include thrombopoietin, reticulated platelets, platelet survival study, bleeding time and serum complement. Coombs test is done to diagnose Evans syndrome which includes autoimmune hemolytic anemia and ITP.

MANAGEMENT:

Treatment should be individualized. Treatment depends mainly on the patients age and the disease severity because as the age increases the risk of bleeding and fatality increases. The primary goal is to keep platelet counts > 30,000/cu mm while minimizing toxicity; as there no increased mortality if platelets are > 30,000/cu mm. This is based on the assumption that:

1) Platelet count is a reliable surrogate marker of bleeding risk
2) Natural history of primary ITP is not altered by medical therapy
3) The burden of disease and its impact in quality of life are adequately captured by bleeding and drug toxicity

When thrombocytopenia occurs secondary to a medical condition treatment should be targeted to correct the underlying disorder. Drugs used to treat ITP either increase the production of platelet, or decrease the production of antibodies or decrease the uptake of antibody coated platelet by the reticuloendothelial system.

CRITERIA FOR TREATMENT:

1) Active bleeding with any platelet count includes intracranial bleed, hematuria, epistaxis, menorrhagia, mucosal bleeding.

2) Platelet count < 10,000

3) Platelet count < 30,000 if the patient has any of the following including platelet dysfunction, surgery, trauma, use of anticoagulants , lifestyle changes with predisposition to injury.[5]

TARGET PLATELET COUNT IN ADULT ITP PATIENTS DURING SURGERY:[5]

SURGERY	RECOMMENDED PLATELET COUNT
Major neurosurgery	≥1,00,000
Major surgery	≥80,000
Minor surgery	≥50,000
Complex dental extraction	≥50,000
Regional dental block	≥30,000
Simple dental procedure	≥30,000
Dental prophylaxis (scaling, deep cleaning)	≥20,000

HOSPITALISATION AND EMERGENCY THERAPY:

Patients with severe major bleeding and platelet <10,000 are hospitalized immediately and given platelet transfusions 15 ml/kg until the bleeding stops and the platelet count exceeds 30,000cells/cu mm. Along with this methylprednisolone 30mg/kg is given intravenously over 20 minutes and intravenous immunoglobulin 1g/kg upto 5 doses may be given. The patient has to be pre-medicated with acetaminophen and diphenhydramine one hour prior to administration of immunoglobulin. Epsilon aminocaproic acid or tranexamic acid can be used to control epistaxis and oral bleed. Fibrin glue and topical thrombin for dental extractions and management of menorrhagia with progestational agents. Patients with intracranial bleed and who require immediate hemostatic response maybe treated with recombinant factor seven a^4 if they do not respond to other modalities of treatment. It is important to stop drugs which cause platelet dysfunction and increase the risk of bleeding and to control blood pressure. Re-check platelet after 24 hours, if it is >20,000 repeat after 7 days or consider re-treatment. If anti-Rh(D) is given do urine analysis, LDH and bilirubin to asses for hemolysis.

DISCHARGE CRITERIA:

1) Stabilized platelet count > 10,000cells/cu mm

2) No age related or social risk factor for head injury. Patients should be counseled regarding contact sports and high risk activities like jumping and diving from height

3) No active bleeding.

INDICATIONS TO TREAT PERSISTENT/CHRONIC ITP:

1. Clinical bleeding
2. Any surgery where there is a need to improve the platelet counts temporarily.
3. Extremely low platelets which increases the risk of bleeding
4. Patients who participate in sports or other high risk endevours.

NEWLY DIAGNOSED ITP- FIRST LINE THERAPY:[5]

Corticosteroids:

Dexamethasone, methylprednisolone or prednisolone can be used for 4-6 weeks. Initial response is seen in 90 to 95% of patients. Sustained response is seen in 5o to 80% of patients. Toxicity depends on the length of administration. Side effects include fluid retention, Cushingoid facies, insomnia, mood swings, anxiety, weight gain, anger, diabetes, GI distress,

ulcers, hypertension, skin changes, alopecia, osteoporosis, immunosuppression, opportunistic infection, adrenal insufficiency. Repeated dosing decreases the tolerability. Short term bolus therapy also lowers the risk of adverse events.

IV Anti-D Immunoglobulin:

Anti-Rh (D) 50-70μg/kg. Initial response rate is 80% and sustained response lasts for 2 to 4 weeks but in some patients it may persist for months. Adverse effects include fever, chills, intra-vascular hemolysis, DIC and renal failure. It should be used only in Rh positive individuals as it acts by producing limited hemolysis. Post infusion the patient should be monitored for 8 hours to observe for severe intravascular hemolysis which occurs rarely.

IV Immunoglobulin:

0.4g/kg/day for 5 days. Rapid response occurs initially in 80% of the patients but is sustained only for 2 to 4 weeks. Side effects include nausea, diarrhea, flushing, fatigue, fever, chills, transient neutropenia, thrombosis, tachycardia, blood pressure changes, tachycardia, aseptic meningitis and renal insufficiency. Anaphylactoid reactions can occur in patients with IgA deficiency. In such patients IgA deficient immunoglobulin can be used.

SECOND LINE APPROACHES:

If the response after initial treatment for one month is not very satisfying and once the patient starts to develop steroid related toxicities second line therapy can be tried. Either monotherapy with danazol or a combination of dapsoneand azathioprine can be tried as steroid sparing agents.

Splenectomy:

The standard line of treatment for ITP patients who do not respond well to prednisolone is Splenectomy. Some have a partial response while two thirds have a long term durable response. Laparoscopic Splenectomy done by experienced surgeons have less mortality and morbidity. Complications include hemorrhage, overwhelming sepsis syndrome, wound infection , thrombosis, sub phrenic abscess, pneumococcal infection, peri-pancreatic necrosis and death .Complications can be reduced by following the recommended vaccination protocols (especially for Hemophilus influenza, pneumococcus and menningococcus) and proper initiation of antibiotics when the first symptoms of a systemic febrile illness appear. Although it is recommended only by few physicians it is cost effective and has the highest chance for long term remission. Long term complications include defective immunity, atherosclerosis and pulmonary hypertension.

Anti-CD20 Antibody: Rituximab 375 mg/m^2 weekly for 4 weeks. Fever, chills and throat scratchiness can occur. Sustained response occurs only in 20 to 30% patients. Severe reactions include anaphylaxis, serum sickness, infection, bronchospasm, pulmonary embolism, infection and retinal artery thrombosis. It may cause fulminant hepatitis in patients with hepatitis b infection and hence is contraindicated in such patients. Rare cases of progressive multifocal leucoencephalopathy has also been reported in patients who are HIV negative with the use of Rituximab.

TRAs (Thrombopoetin receptor agonists):Romiplostin, eltrombopag are the two FDA approved TRAs used in primary ITP in patients who need continuous treatment after the initial course of corticosteroids.

Romiplostin is a peptide given subcutaneously which prolongs the half-life of the thrombopoietin receptor. Many patients who were given this drug had a better quality of life as they could discontinue corticosteroids.

Eltrombopag is an oral drug which reduced the need for rescue therapy.

Both these drugs might lead to increased reticulin deposition in the bone marrow and may ultimately lead to bone marrow fibrosis. Certain trials have demonstrated a rebound thrombocytopenia in about 10% of the patients with the discontinuation of these drugs. Some studies have demonstrated

increased risk of venous thrombosis especially in hepatitis c virus positive individuals who take eltrombopag. Periodic ophthalmologic examinations and liver function tests should also be done in patients taking eltrombag as they are known to cause hepatobiliary abnormalities and cataract. These agents are mainly used for refractory cases of ITP.

THIRD LINE THERAPY:

Immunosuppressive drugs like azathioprine, mycophenolate mofetil, cyclosporine and cyclophosphamide; used either alone or in combination has been tried in patients not responding to either the first line or second line therapies. They have very little efficacy. Hematopoietic stem cell transplantation and drugs like vinca alkaloids are tried only for resistant cases. These drugs have a very limited safety profile and hence only tried as a last resort for unresponsive patients.

CRITERIA TO ASSESS TREATMENT RESPONSE IN ADULT ITP:

Complete response: When after treatment the platelet count is at least 1,00,000 cells/cu mm. and there should be no bleeding.

Response: When the baseline platelet count doubles and the platelet counts should be in the range between 30,000 to 1,00,000cells/ cu mm. ,in the absence of bleeding.

Time to response is defined as the time when the treatment is started to the time when the patient achieves either complete response or response. The time to assess response depends on the type of treatment.

INITIAL AND PEAK RESPONSE FOR DIFFERENT AGENTS:[3]

AGENT	INITIAL RESPONSE(Days)	PEAK RESPONSE(Days)
Prednisolone	4-14	7-28
Dexamethasone	2-14	4-28
IV Ig	1-3	2-7
Anti-D	1-3	3-7
Rituximab	7-56	14-180
Splenectomy	1-56	7-56
Danazol	14-90	28-128
Azathioprine	30-90	30-180
Vincristine	7-14	7-42
Eltrombopag	7-28	14-90

No response: there is no doubling of the baseline platelet count and the platelet count continues to be <30,000 cells/cu mm or the patient continues to bleed.

Duration of response: It is measured as the time interval between the achievement of complete response or response to the loss of complete response or response. It is measured as the proportion of cumulative time the patients spends in complete response or response during the period under examination.

Corticosteroid dependence: when there is ongoing need for continuous administration of steroids or the patient needs frequent course of steroids to avoid bleeding or to maintain platelets ≥30,000cells/ cu mm. Patients who are dependent on steroids or other treatment modalities are considered as non-responders.

REFRACTORY ITP:

The patients are labeled as refractory cases if they meet all the following criteria

1) Patients who fail to achieve response after splenectomy or if they relapse.

2) Patients who have severe ITP or risk of major bleeding which requires treatment. Need of adjunctive or on demand therapy will not qualify the patient as refractory. On demand therapy is defined as one in which the platelet count is temporarily increased in case of a major bleed or trauma or sufficiently safety levels to perform any invasive procedures. Any non-ITP specific therapy used to decrease bleeding like platelet transfusion, hormonal agents, anti-fibrinolytic drugs desmopressin, fibrin sealants etc are considered as adjunctive treatment.

3) Primary ITP confirmed after exclusion of other secondary causes of thrombocytopenia.

Response to therapy in refractory ITP is defined as ability to maintain platelet count to prevent significant bleeding. They represent only < 10% of adult ITP.

HELICOBACTER PYLORI AND ITP[5]:

As the detection and the eradication of H.pylori is inexpensive, safe and well tolerated it has been proposed as a routine test in the initial evaluation of patients with ITP. This is considered appropriate in areas where the H.pylori infection prevalence is high. Further investigations and studies are required to prove the relationship between ITP and H.pylori.

HELICOBACTER PYLORI: INTODUCTION:

Warren and Marshell from Australia observed spiral, campylobacter like bacteria in close apposition to the gastric mucosa in several cases of gastritis and peptic ulcer. They named it Campylobacter pylori. Since they had several characters which were different from Campylobacter they were renamed later as Helicobacter pylori.

HELICOBACTER PYLORI: MORPHOLOGY

It is a gram negative spiral rod which is motile by a unipolar tuft of lophotrichous flagella. It grows on chocolate agar under microaerophilic conditions with pH 6 to 7 and CO_2 5-20%.It produces oxidase, catalase, phosphatase and H_2S. H.pylori resides in the gastric mucus and it has several acid resistant mechanisms to protect itself. It has the unique property of producing urease, which hydrolyses urea to form ammonia which acts as a buffer in the acidic medium of the stomach.

There are several non-pylori gastric helicobacters which are acquired as zoonosis. There are also non gastric Helicobacter (intestinal) which includes H.cinnaedi and H.fennelliae and cause proctitis in HIV patients. Colonization with H.pylori is a risk factor for peptic ulcer disease (both gastric and duodenal ulcers), gastric MALT lymphoma and gastric adenocarcinoma. Recent studies have shown that H.pylori colonization is a risk factor for iron deficiency anemia, rheumatoid arthritis, ITP etc. It is shown to be protective against asthma, obesity and GERD.

EPIDEMIOLOGY: The prevalence in developing countries is >80% and in developed countries it is around 30%. The prevalence increases with age. Infection is usually acquired in childhood. Risk factors for colonization of H.pylori include over-crowding and maternal colonization the low incidence in children of developed countries is due to increased use of antibiotics and decreased rates of maternal colonization. The only important reservoir of H.pylori is humans. Infection is usually acquired by the feco-oral route

PATHOLOGY AND PATHOGENESIS:

H.pylori causes a chronic superficial gastritis in which there is infiltration of the gastric mucosa by polymorphonuclear and mononuclear cells. There is a chronic persistent immune response due to H.pylori colonization. It activates

both humoral and cell mediated immune responses. Both and systemic antibodies are produced. However the bacterium is not cleared, this is because H.pylori down regulates the immune system.

Every person colonized by H.pylori is not symptomatic only a few develop overt disease. This is due to certain host factors, environmental factors and bacterial strain differences .Certain virulence factors include CagA, VacA, adhesins such as BabA, SabA and DupA. CagA induces inflammatory, cytoskeletal and proliferative changes. It also affects the host cell signal transduction. This leads to gastric inflammation and peptic ulcer disease and gastric adenocarcinoma.

Host factors include genetic polymorphisms of cytokine genes and genes that encode for toll like receptor. Environmental factors include smoking, high salt diet and preserved food. Diet rich in anti-oxidants and vitamin C are protective.

Pan gastritis and corpus predominant gastritis leads to gastric ulceration and adenocarcinoma whereas antral predominant gastritis leads to duodenal ulcer. Somatostatin reduces gastrin levels. H.pylori inflammation leads to depletion of somatostatin producing D cells hence during meals more secretions are produced which leads to antral inflammation. The

pathogenesis of gastric adenocarcinoma is not clear as hypochlorhydria occurs despite hypergastrinemia. The following sequence occurs in intestinal type of adenocarcinoma, initially there is simple gastritis then gastric atrophy leading to intestinal metaplasia and dysplasia. Chronic gastritis leads to diffuse type of adenocarcinoma.

Pathogenesis in H.pylori and ITP:

Molecular mimicry is the most popular hypothesis to explain the mechanism by which ITP is triggered by H.pylori infection. It induces antibody production against certain antigens which cross react with the platelet antigens[7].The antigen most commonly implicated is CagA and once H.pylori is eradicated, antibodies against CagA disappear from serum .This is supported by studies from Italy where Cag A gene positivity was more prevalent in ITP patients than the control group. Another hypothesis is the induction of Th1 phenotype which favors the onset and persistence of ITP[8]. CagA positive strains may be more prevalent in developing word and less prevalent in the developed countries. These genotypic variations in distribution might explain why response is seen only in certain geographic areas .Some studies have shown that presence of H.pylori antibodies causes platelet aggregation by binding to Von Willibrand's factor and inducing glycoprotein 1b[8]. There are several alternative theories and none are

mutually exclusive. Confirmatory studies are still needed to confirm these hypotheses.

Genome:

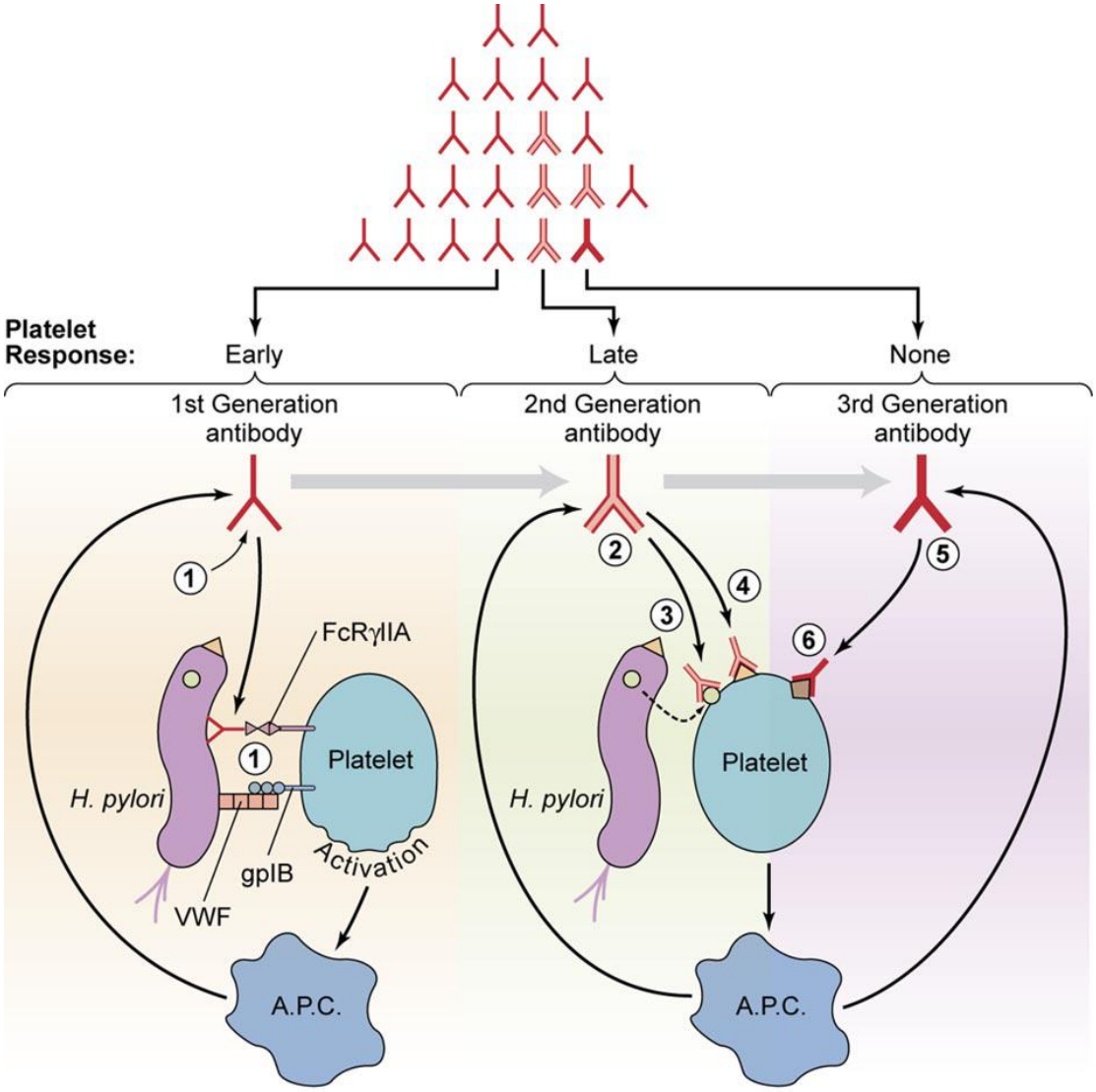
H.pylori consists of a large diversity of strains, and the genomes of three have been completely sequenced. The genome of the strain "26695" consists of about 1.7 million, base pairs with some 1,550 genes. The two sequenced strains show large genetic differences, with up to 6% of the nucleotides differing.

Study of the *H. pylori* genome is mainly centered on attempts to understand pathogenesis that is, the ability of this organism to cause disease. Approximately 29% of the loci are in the "Pathogenicity Island". Two of sequenced strains have a very long Cag pathogenicity island (a common gene sequence believed responsible for pathogenesis) that contains over 40 genes. This pathogenicity island is usually absent from *H. pylori* strains isolated from humans who are carriers of *H. pylori*, but remain asymptomatic.

The *CagA* gene codes for one of the major *H. pylori* virulence proteins. Bacterial strains that have the CagA gene are associated with an ability to

cause ulcers. The CagA gene codes for a relatively long protein. The *cag* pathogenicity island has about 30 genes, which code for a complex secretion system.

Types of Anti-bodies:



Generation of three types of antibodies has been proposed:

1) H.pylori antibodies bind to Von Willibrand's factor and platelet glycoprotein. So platelets get activated and are cleared.

2) Somatic mutation of the organism leads to formation of second generation antibodies. They either detects the bacterial protein bound to the platelet or cross react with the platelet antigens. At this stage the patient responds to therapy with antibiotics.

3) Patients who are not responsive to therapy develop further somatic mutation which leads to formation of third generation of antibodies. These antibodies lose their activity against the organism but retain their activity against the platelets.

CLINICAL FEATURES:

H.pylori is the main cause of peptic ulcer disease both gastric and duodenal ulcer. It also is responsible for non-cardia adenocarcinoma of stomach and primary gastric lymphoma. Functional or non-ulcer dyspepsia is one in which patient has symptoms pertaining to the upper gastrointestinal system but upper gastrointestinal endoscopy shows normal results. The association of H.pylori with dyspepsia is not clear. H.pylori seems to have a protective role in GERD, Barrett’s esophagus and adenocarcinoma of gastric cardia and

esophagus. Pernicious anemia and autoimmune gastritis are also precipitated by H.pylori. It also leads to iron deficiency anemia by causing occult blood loss, reducing iron absorption and causing hypochlorhydria.

H.pylori has also been implicated in certain extra-gastrointestinal pathologies. But the evidence of causality is less strong, included under this are ITP, coronary artery disease and cerebrovascular disease. Recent studies have shown a protective role of $CagA^+$ H.pylori in childhood asthma, atopic disorders and hay fever[1].

DIAGNOSIS:

Two groups of tests are available, invasive tests in which endoscopy tests are done and biopsy samples are analyzed and noninvasive tests. Endoscopy is usually done for older patients in whom adenocarcinoma is suspected, it is never the initial procedure of choice for young patients with dyspepsia. Once endoscopy is performed two biopsy specimens are taken from the antrum. They can be subjected to histological examination which is more accurate in identifying H.pylori. Specials stains like silver stain or modified Geimsa stains are available which helps in optimal visualization of the organism. It also provides additional information like the degree and pattern of inflammation, atrophy, metaplasia and dysplasia. The biopsy urease test is

the most convenient biopsy based test. The biopsy specimens are placed in a gel containing urea and an indicator. pH alteration occurs if H.pylori urease is present and this leads to color change, and it usually occurs in minutes but may take as long as 24 hours. Cultures can be done and H.pylori confirmed by its typical appearance on gram stain and positive biochemical tests like oxidase, catalase and urease. Culture has the advantage that the organisms' antibiotic sensitivity can be determined and can be useful clinically.

Non-invasive tests include the urea breath test which is accurate. The patients drinks a solution containing urea labeled nonradioactive ^{13}C and later blows into a tube .If H.pylori urease is present then it will hydrolyze urea and labeled carbon dioxide will be detected in blood samples. The stool antigen test is less expensive, more convenient and simple assay but is slightly less accurate when compared to the urea breath test. Serological assays using immunoblot or enzyme linked immunosorbent assay to detect H.pylori specific IgG antibodies are also available.

Success to treatment can be assessed using the biopsy based tests, stool antigen tests and the urea breath tests. Serological tests cannot be used to monitor treatment because it takes time for the H.pylori specific antibodies to drop and it not practical to monitor this gradual fall in H.pylori antibodies. All these tests are dependent on the H.pylori load and hence the patient

should be off any antibiotics when they are done or it may be false negative. Similarly follow up endoscopy is a must in patients with gastric ulcer to see if the ulcer has healed and to monitor for gastric carcinoma.

COMMONLY USED TESTS TO DETECT H.PYLORI:

TEST	ADVANTAGES	DISADVANTAGES
INVASIVE (based on endoscopic biopsy)		
Rapid urease test	Simple and quick	Some tests are not fully sensitive before 24 hours
Histology	Gives additional information	Sensitivity depends on use of special stains and experience
Culture	Antibiotic susceptibility determined	Sensitivity depends on experience
NONINVASIVE		
Serology	Convenient, cost	Not used for follow

	effective. Not effected by PPIs or antibiotics	up and is less accurate.
^{13}C urea breath test	Simple, inexpensive, used for follow up	Not very convenient, requires fasting.
Stool antigen test	Convenient, cost effective, used for follow up.	Disliked by people, less accurate

Indications to treat H.pylori include gastric or duodenal ulcer or any low grade B cell lymphoma. Monotherapy is usually not indicated because of inadequate delivery of antibiotic to the colonization niche. Hence triple and quadruple regimens are used which have eradication rates > 90% Recently

PPIs and ranitidine bismuth citrate and two or three antibiotics are used for7 to 14 days. Successful H.pylori treatment depends upon two main factors the compliance of the patients and the use of antibiotics to which the infecting strains are susceptible.

TREATMENT REGIMENS RECOMMENDED FOR H.PYLORI:

REGIMEN	DRUG 1	DRUG 2	DRUG 3	DRUG 4
OCA 7 to 14 days	Omeprazole 20mg bid	Clarithromycin 500mg bid	Amoxicillin 1g bid	
OCM 7 to 14 days	Omeprazole 20mg bid	Clarithromycin 500mg bid	Metronidazole 500mg bid	
OBTM 14 days	Omeprazole 20mg bid	Bismuth subsalicylate 2tablets qid	Tetracycline HCl 500mg qid	Metronidazole 500mg tid
sequential (5 d + 5 d)	Omeprazole 20mg bid	Amoxicillin 1g bid		
	Omeprazole 20 mg bid	Clarithromycin 500mg bid	Tinidazole 500 mg bid	
5.- OAL 10 days	Omeprazole 20mg bid	Amoxicillin 1 g bid	Levofloxacin 500mg qid	

PREVENTION :

Proper sanitation

Good personal hygiene.

Hygienic food habits

Vaccination

Prevent overcrowding

INFECTION INDUCED THROMBOCYTOPENIA:

The most important cause for non iatrogenic thrombocytopenia is due to viral and bacterial infections. Most Gram negative sepsis are associated with DIC Infections can affect both platelet production and platelet survival. There is also immune mediated platelet destruction. In children ITP is usually due to viral infection. A bone marrow examination is usually done in occult infections.

DRUG INDUCED THROMBOCYTOPENIA:

Use of many drugs has been associated with thrombocytopenia. many chemotherapeutic agents, over the counter drugs and herbal drugs have been implicated. Classic drug induced antibodies against the platelets have been

detected mainly against chloroquine and sulphonamides. The thrombocytopenia typically occurs within 21 days of drug exposure and the patient recovers within 10 days of stopping the drug. Abciximab differs from other drugs in that the thrombocytopenia typically occurs within 24 hours of exposure. The drugs are given below:

Acetaminophen, Aminosalicyclic acid ,Amiadarone ,Ampicilin ,Carbamezepine ,Danazol ,Diclofenac ,Digoxin ,Ethambutol ,Frsemide ,Imipenem/cilastatin ,Ibuprofen ,Linezolid ,Methydopa, Phenytoin, Rifampin,Valproic acid, Vancomycin, Sulpha group of drugs.

HEPARIN INDUCED THROMBOCYTOPENIA:

It differs from other drug induced thrombocytopenia in two ways:

1) It does not cause severe thrombocytopenia that is platelet counts < 20,000

2) It does not cause bleeding but is instead associated with increased risk of thrombosis

Here antibodies are formed against platelet factor 4 and the platelet gets activated and is removed by the reticuloendothelial system it occurs after exposure to both unfractionated heparin and low molecular weight heparin

Platelets drop 5 to 15 days after exposure. The four T's associated with HIT include:

Timing of exposure

Thrombosis

Thrombocytopenia and

Other causes of low platelet not evident.

The antibodies produced can be detected by ELISA.

Heparin should be stopped and other drugs like argatroban and lipuridin which are direct thrombin inhibitors should be used.

INHERITED THROMBOCYTOPENIA:

It can be autosomal dominant, autosomal recessive or X- linked pattern.

AD ; Common feature is large platelets.It includes May Hegglin anomaly and Sebastin, Epsteins and Fechtner syndrome.

AR includes Bernard Soulier syndrome, Thrombocytopenia with absent radii. Congenital amegakaryocytic thrombocytopenia.

X linked include Wiskott Aldrich syndrome and dyshematopeotic syndrome

MATERIALS AND METHODS

SETTING

This study is conducted in the Medicine department of Madras medical college in collaboration with Department of Hematology and Department of Gastroenterology along with the support of the Pathology, Biochemistry and Microbiology departments.

ETHICAL APPROVAL

Obtained.

STUDY DURATION

This study was conducted over a period of 6 months.

STUDY POPULATION

Patients admitted with acute onset ITP in the medical wards and ITP patients who are on regular follow up in the Hematology department of Rajiv Gandhi Government General Hospital.

TYPE OF STUDY

Cross sectional study.

INCLUSION CRITERIA

Patients with ITP in whom the secondary causes of ITP have been ruled out

EXCLUSION CRITERIA

APLA

HIV patients

Hepatitis C virus positive patients

SLE

Lymphoproliferative disorders

Drug induced thrombocytopenia

Children < 10 years

Pregnant women

Chronic renal disease

Chronic liver disease patients

Pseudothrombocytopenia

SLE

SAMPLE SIZE

50 patients with ITP who are stable with no active bleeding and stable platelet counts.

METHODS

Patients with ITP on regular follow up in the Hematology Department of the Rajiv Gandhi Government General Hospital will be asked questions as per a questionnaire and will be subject to clinical examination. All the secondary causes of ITP will be ruled out using appropriate tests. Patients will be grouped as per age, sex and platelet counts. Patients who have dyspeptic symptoms will be identified. Routine lab investigations will be done. Platelets counts will be done before endoscopy. Patients with stable platelet counts and no active bleeding will then be subject to Upper GI endoscopy in the Medical Gastroenterology Department and the findings will be recorded. A biopsy will be taken from the antrum and the biopsy will be subject to Rapid urease test to detect H.pylori. Patients who turn out to be positive will be put on H.pylori regimen

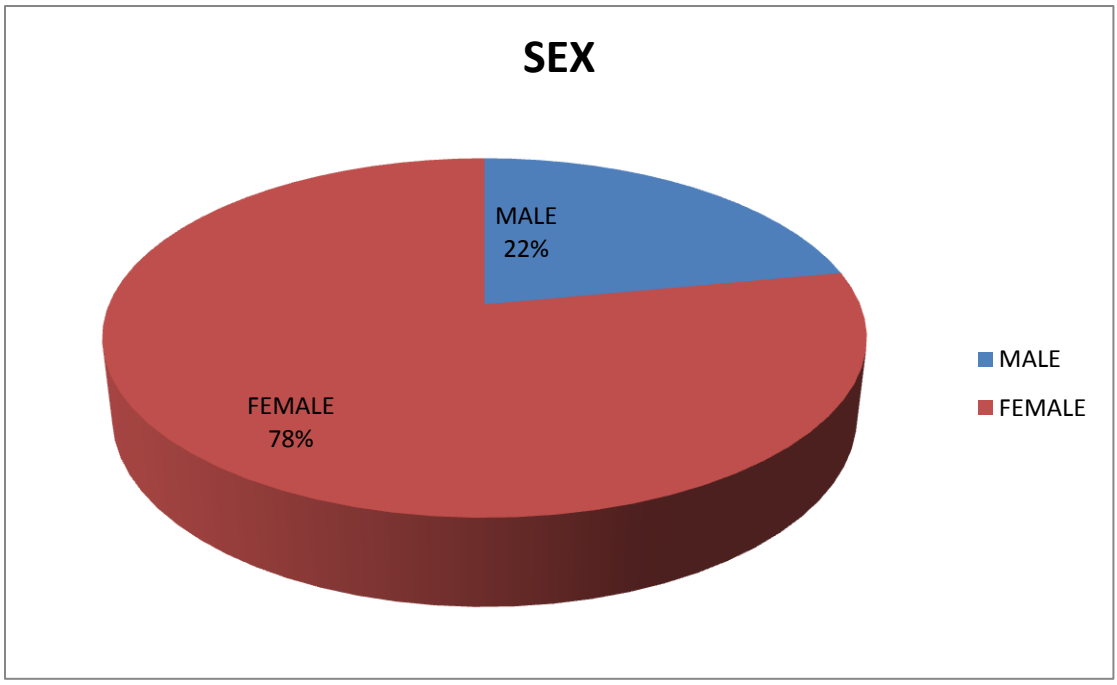
STATISTICAL ANALYSIS:

Results were analyzed using chi square test and Fischer's exact t test.

OBSERVATION AND RESULTS

SEX AND ITP:

SEX	FREQUENCY	PERCENTAGE
MALE	11	22
FEMALE	39	78

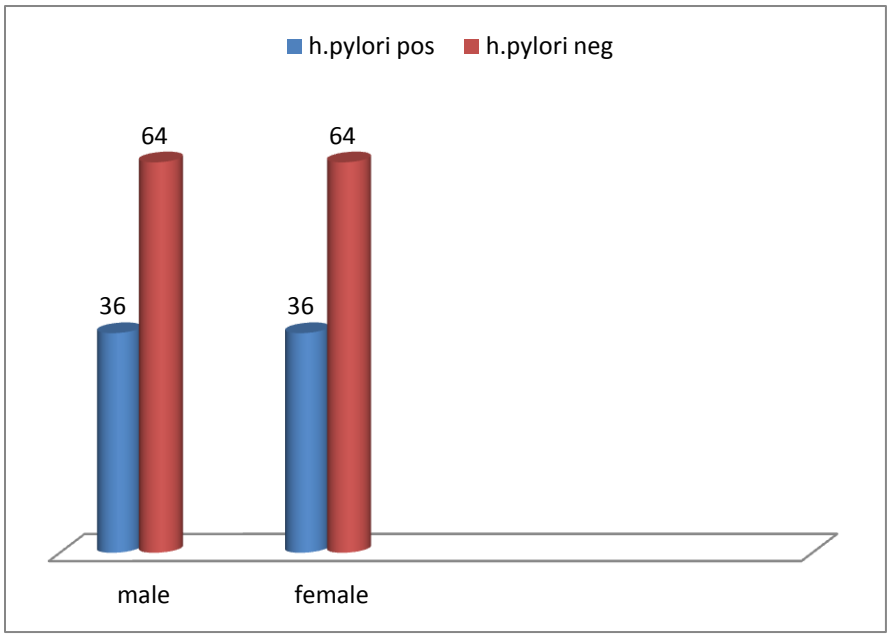


Male to female ratio: 1:3.5.

SEX AND H.PYLORI POSITIVITY:

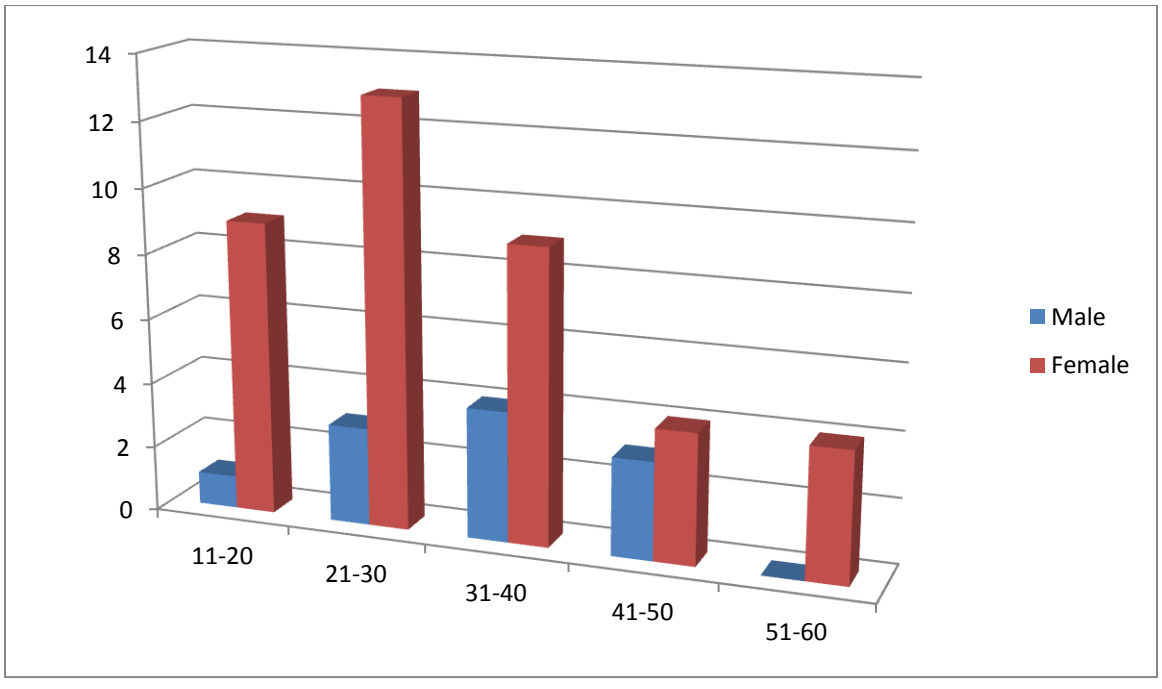
SEX	FREQUENCY	HP POSITIVE	HP NEGATIVE
MALE	11	4(36%)	7(64%)
FEMALE	39	14(35.89%)	25(64.1%)

P value is 1(not significant)



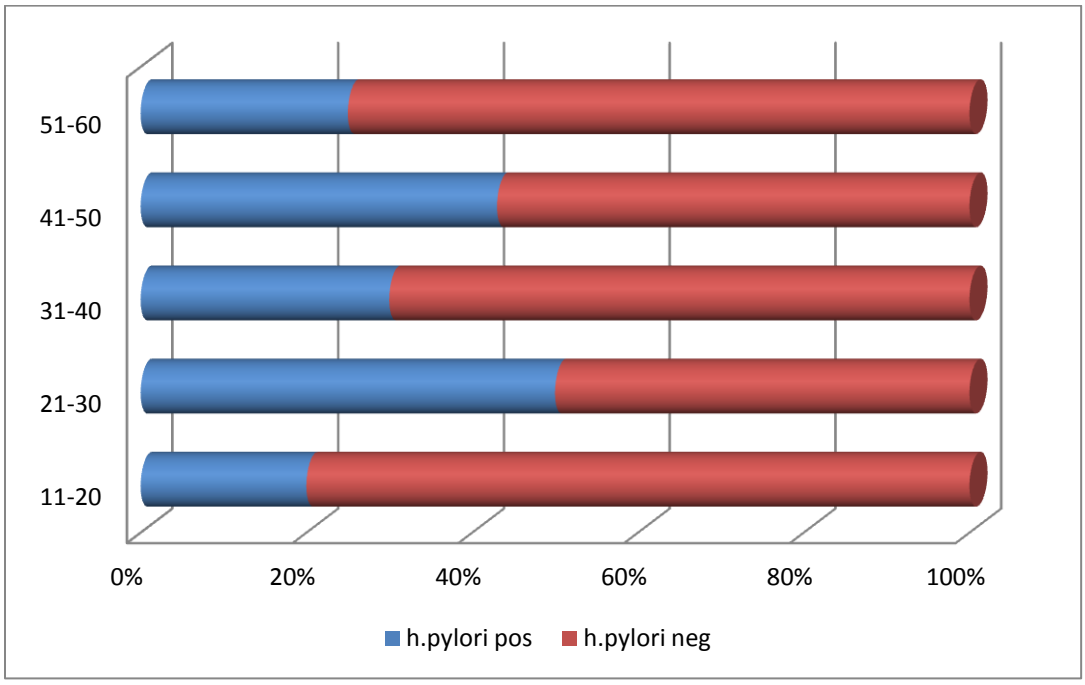
AGE AND ITP:

AGE	FREQUENCY	PERCENTAGE	MALE	FEMALE
11-20	10	20	1	9
21-30	16	32	3	13
31-40	13	26	4	9
41-50	7	14	3	4
51-60	4	8	-	4



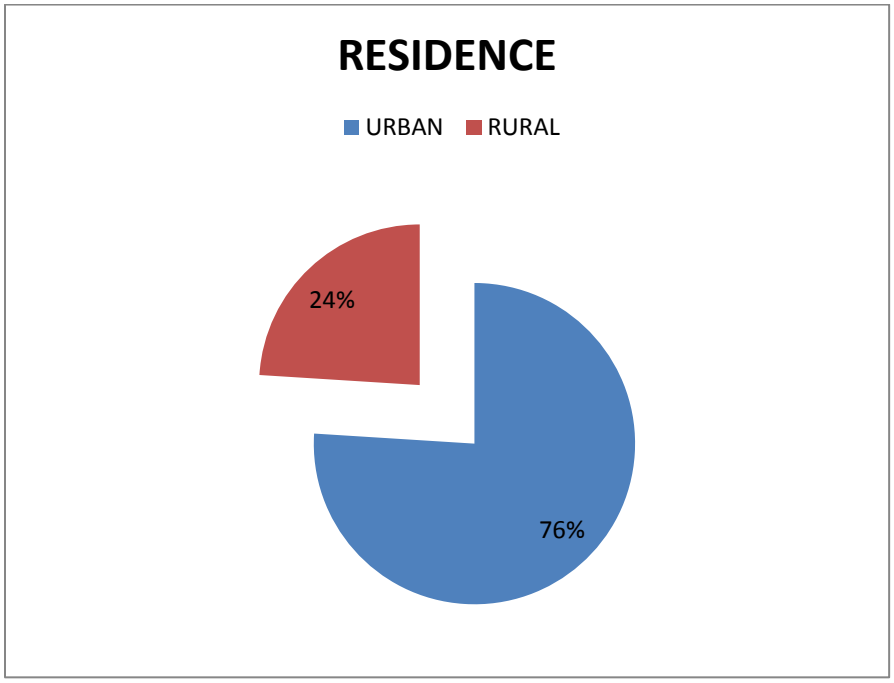
H.PYLORI POSITIVITY WITH RELATION TO AGE:

AGE	FREQUENCY	HP POSITIVE	HP NEGATIVE
11-20	10	2	8
21-30	16	8	8
31-40	13	4	9
41-50	7	3	4
51-60	4	1	3



RESIDENCE AND ITP:

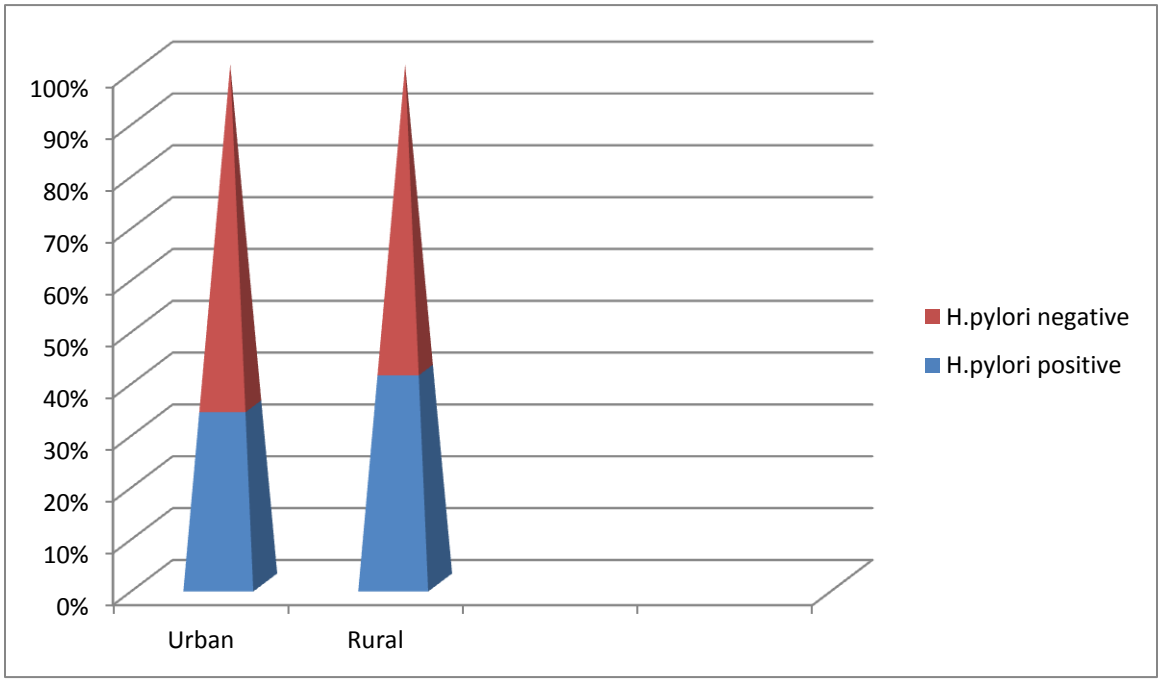
RESIDENCE	FREQUENCY	PERCENTAGE
URBAN	38	76%
RURAL	12	24%



H.PYLORI POSITIVITY WITH RELATION TO RESIDENCE:

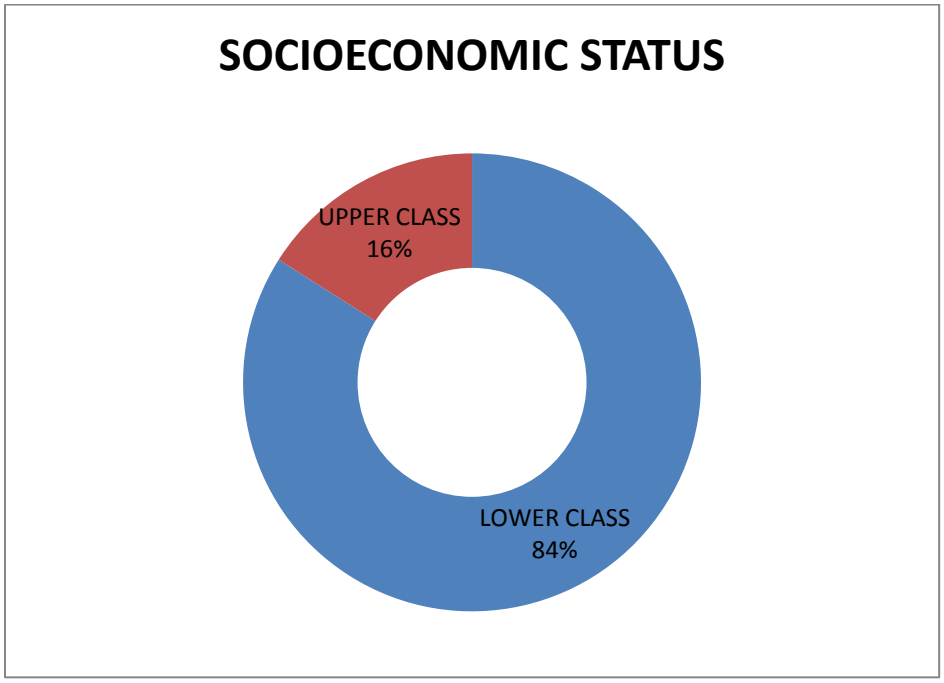
RESIDENCE	FREQUENCY	HP POSITIVE	HP NEGATIVE
URBAN	38	13(34%)	24(66%)
RURAL	12	5(41%)	8(59%)

P value is 0.7(not significant)



SOCIOECONOMIC STATUS AND ITP:

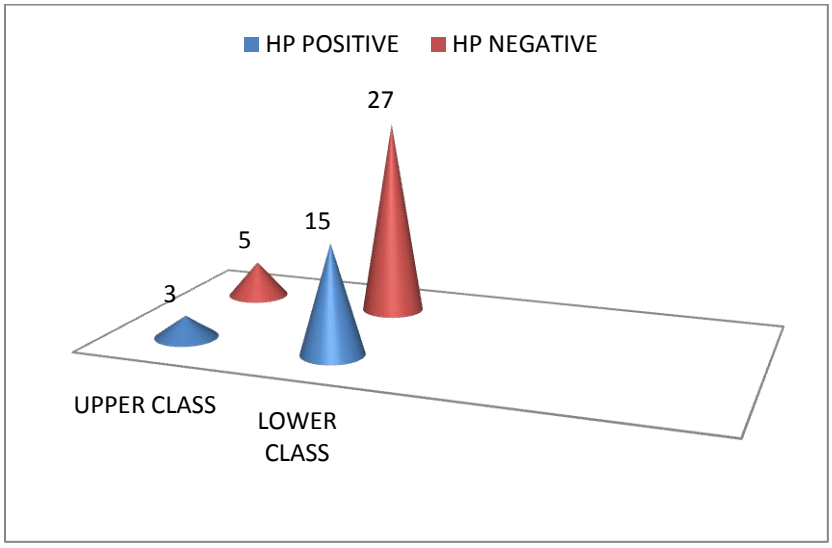
SES	FREQUENCY	PERCENTAGE
LOWER CLASS	42	84
UPPER CLASS	8	16



H.PYLORI POSITIVITY AND SOCIOECONOMIC STATUS:

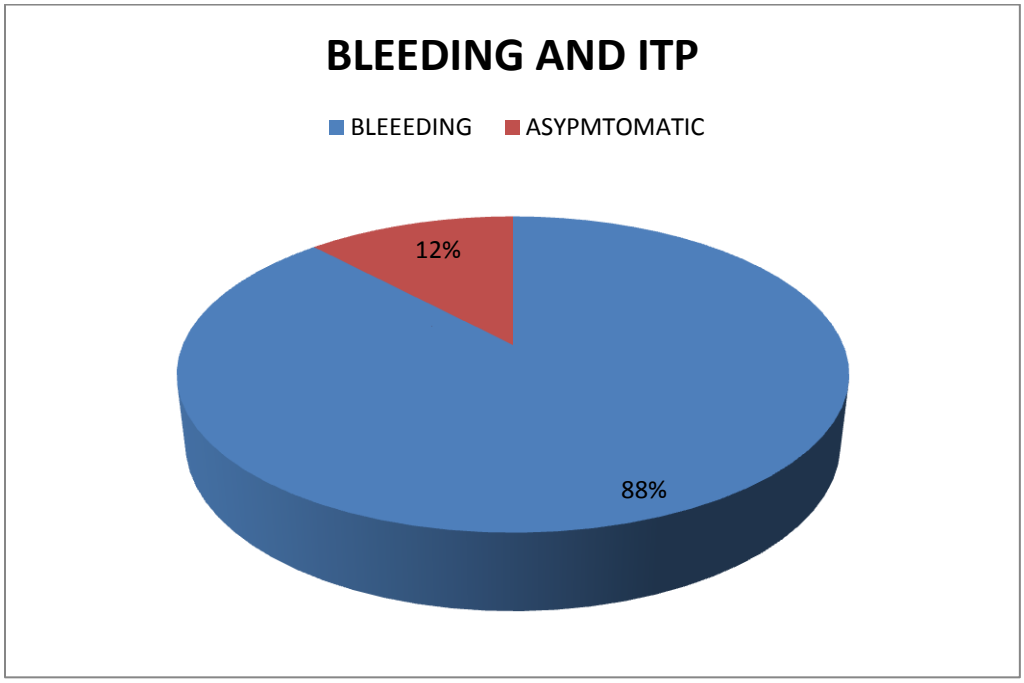
SES	FREQUENCY	HP POSITIVE	HP NEGATIVE
LOWER CLASS	42	15(36%)	27(64%)
UPPER CLASS	8	3(37%)	5(63%)

P value is 1(not significant)



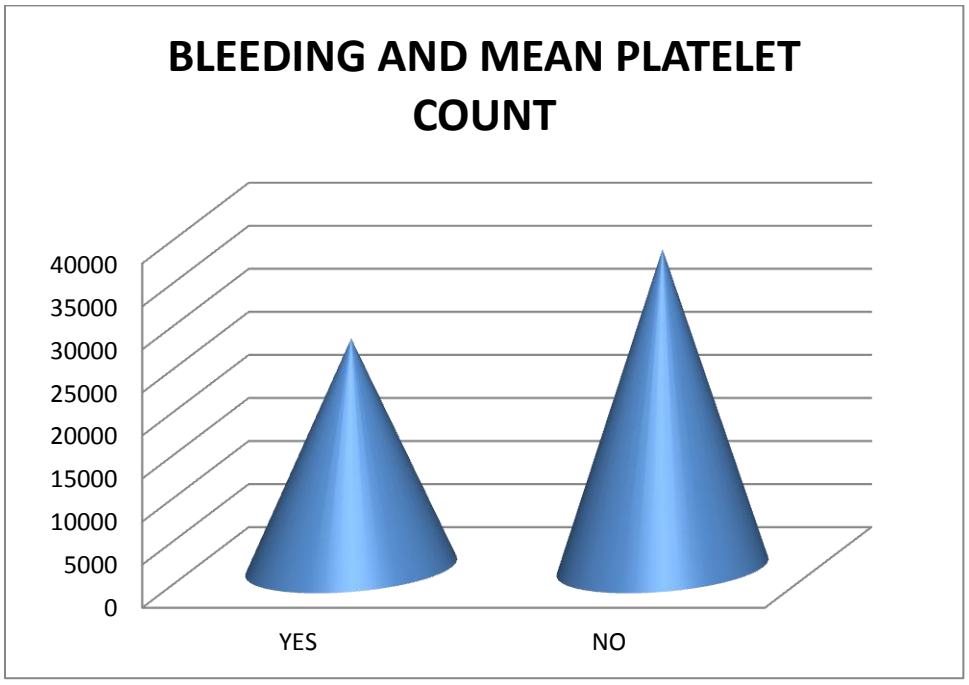
BLEEDING AND ITP:

BLEEDING	FREQUENCY	PERCENTAGE
YES	44	88
NO	6	12



MEAN AGE AND MEAN PLATELET COUNT IN ITP PATIENT WITH AND WITHOUT BLEEDING:

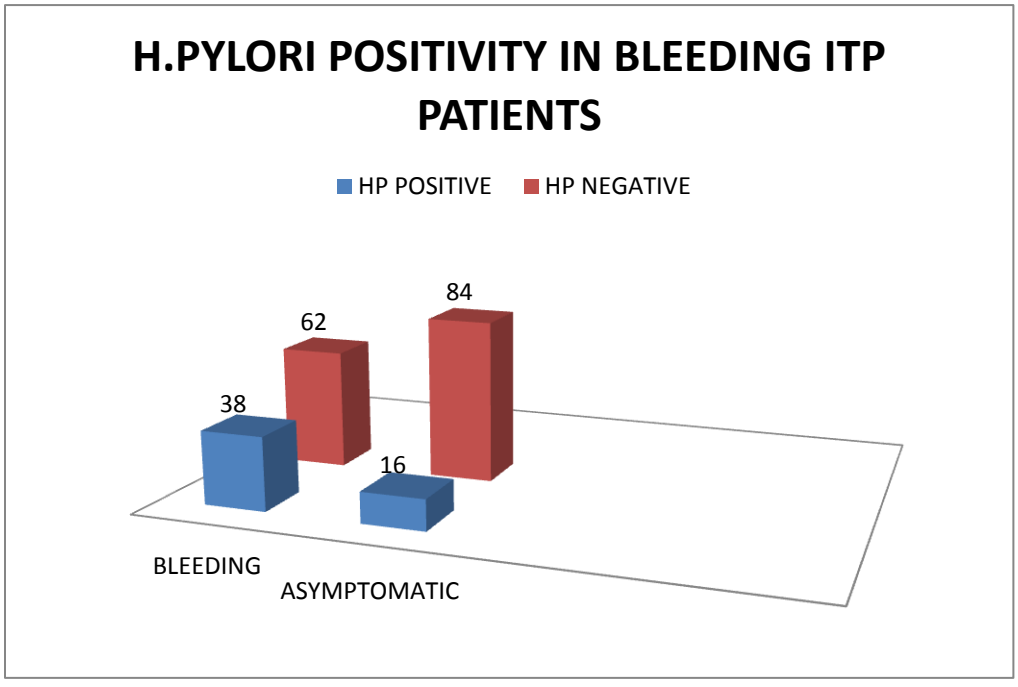
BLEEDING	MEAN AGE (YEARS)	MEAN PLATELET COUNT
YES	32.54	26613
NO	27	37000



H.PYLORI POSITIVITY IN BLEEDING ITP PATIENTS:

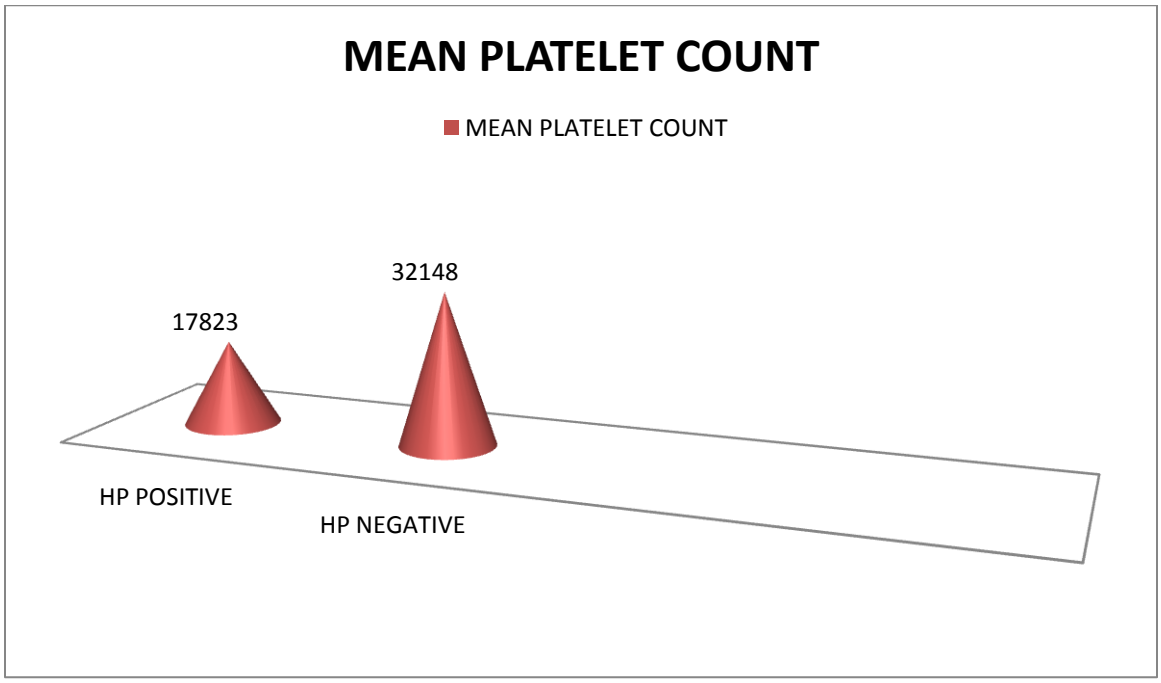
BLEEDING	FREQUENCY	HP POSITIVE	HP NEGATIVE
YES	44	17(38%)	27(62%)
NO	6	1(16%)	5(84%)

P value is 0.3(not significant).



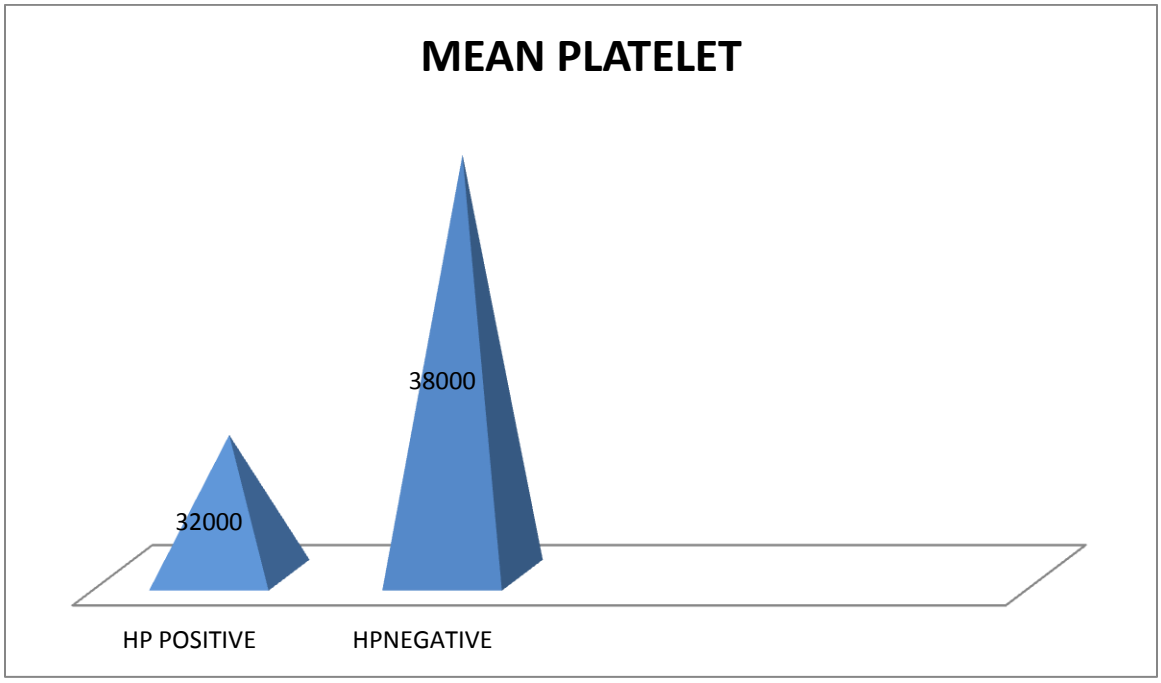
MEAN PLATELET COUNT IN PATIENTS WITH BLEEDING AND H.PYLORI POSITIVITY:

BLEEDING	HP POSITIVE	MEAN PLATELET COUNT
YES	17	17823
NO	1	32000



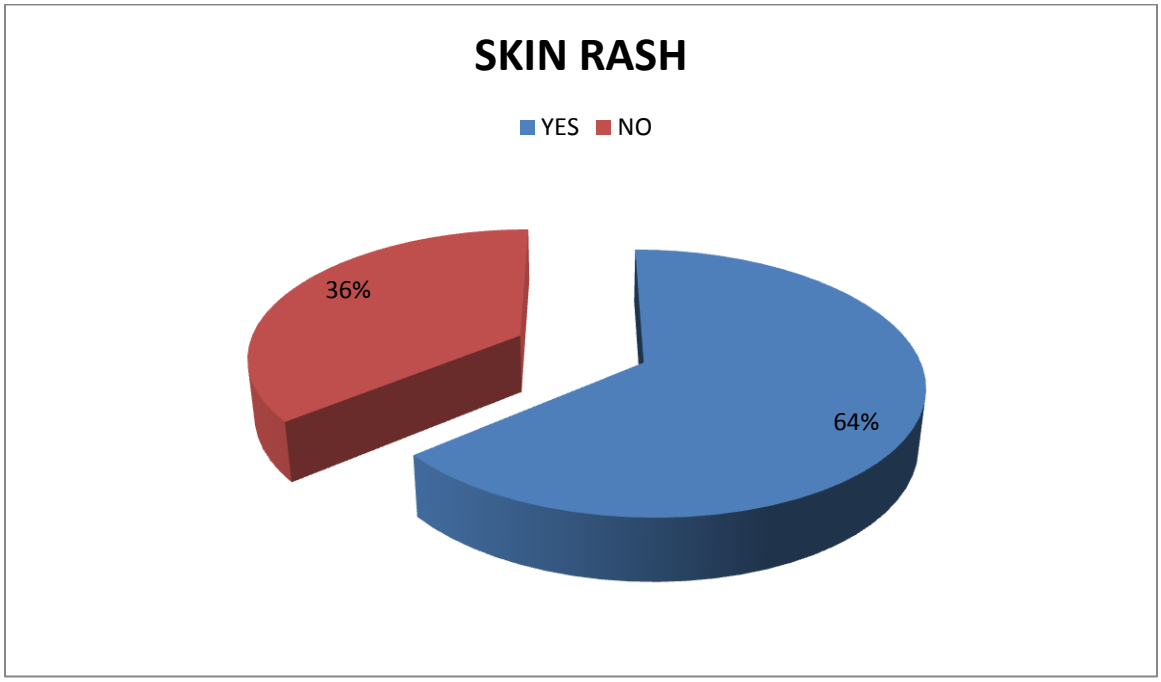
MEAN PLATELET IN ASYMPTOMATIC H.PYLORI POSITIVE PATIENTS:

	NO BLEEDING	MEAN PLATELET
HP POSITIVE	1	32000
HP NEGATIVE	5	38000



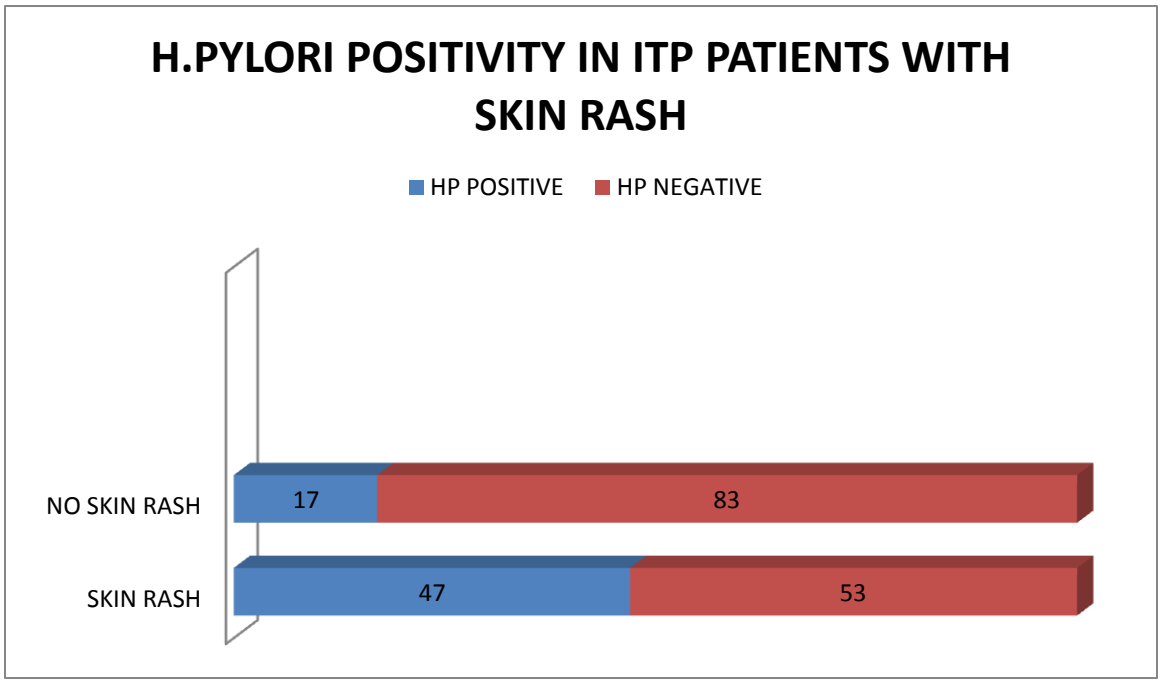
SKIN RASH AND ITP:

SKIN RASH	FREQUENCY	PERCENTAGE
YES	32	64
NO	18	36



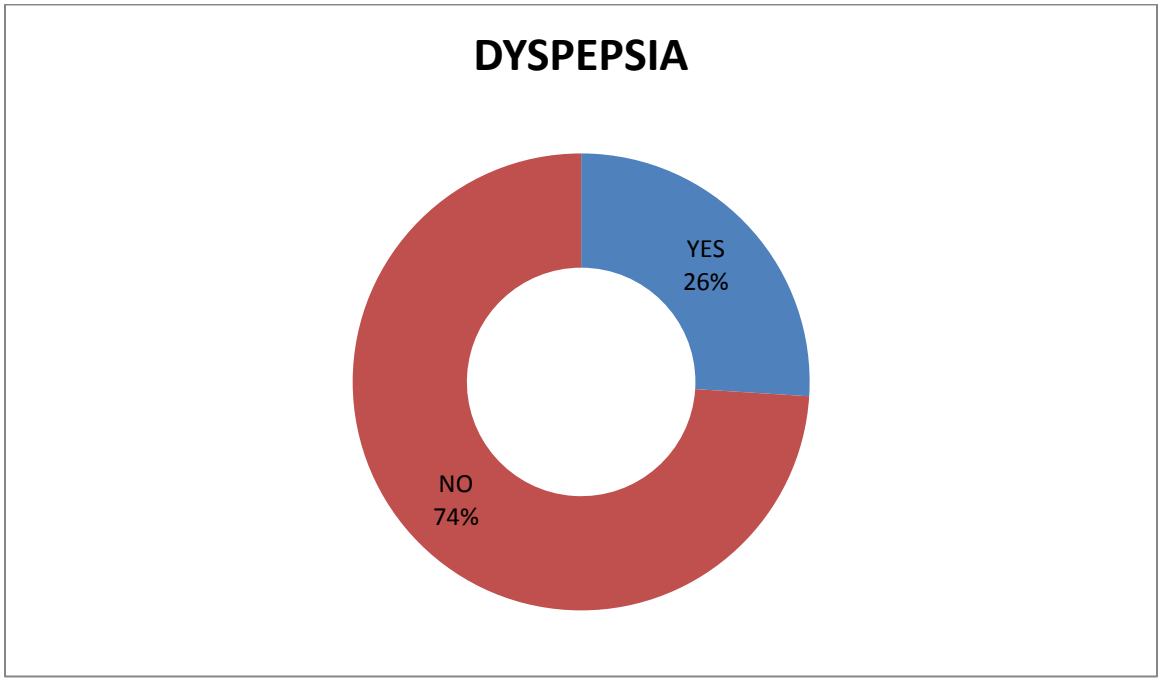
H.PYLORI POSITIVITY AND SKIN RASH IN ITP:

SKIN RASH	HP POSITIVE	HP negative
YES	15(47%)	27(53%)
NO	3(17%)	15(83%)



DYSPEPSIA AND ITP:

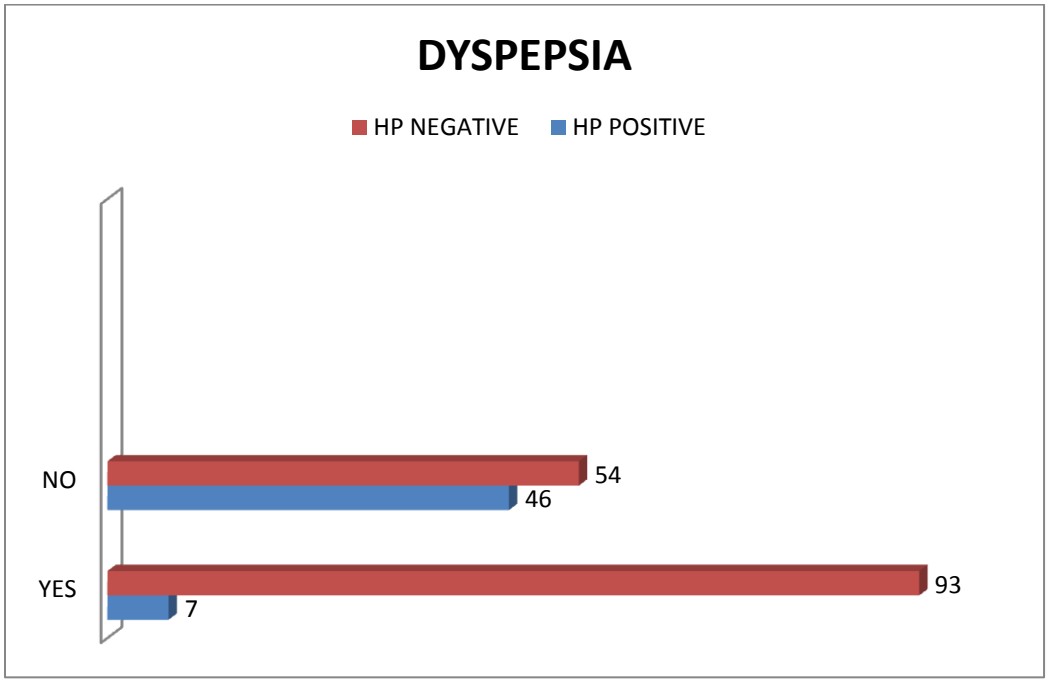
DYSPEPSIA	FREQUENCY	PERCENTAGE
YES	13	26
NO	37	74



DYSPEPSIA AND H.PYLORI POSITIVITY IN ITP:

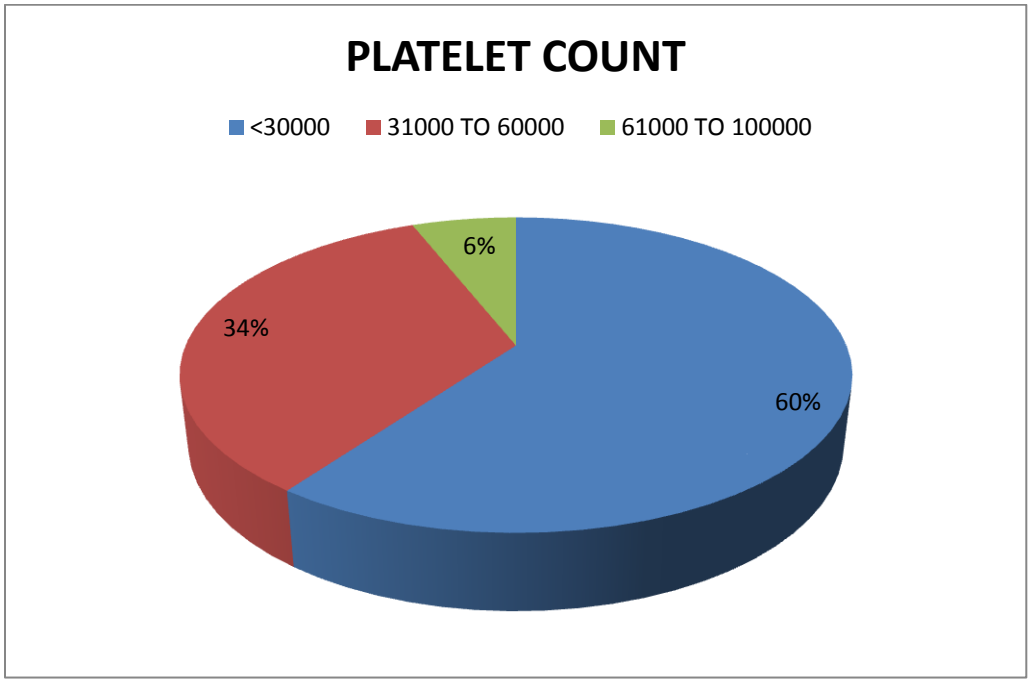
DYSPEPSIA	FREQUENCY	HP POSITIVE	HP NEGATIVE
YES	13	1(7%)	12(93%)
NO	37	17(46%)	20(54%)

P value is 0.3 (not significant)



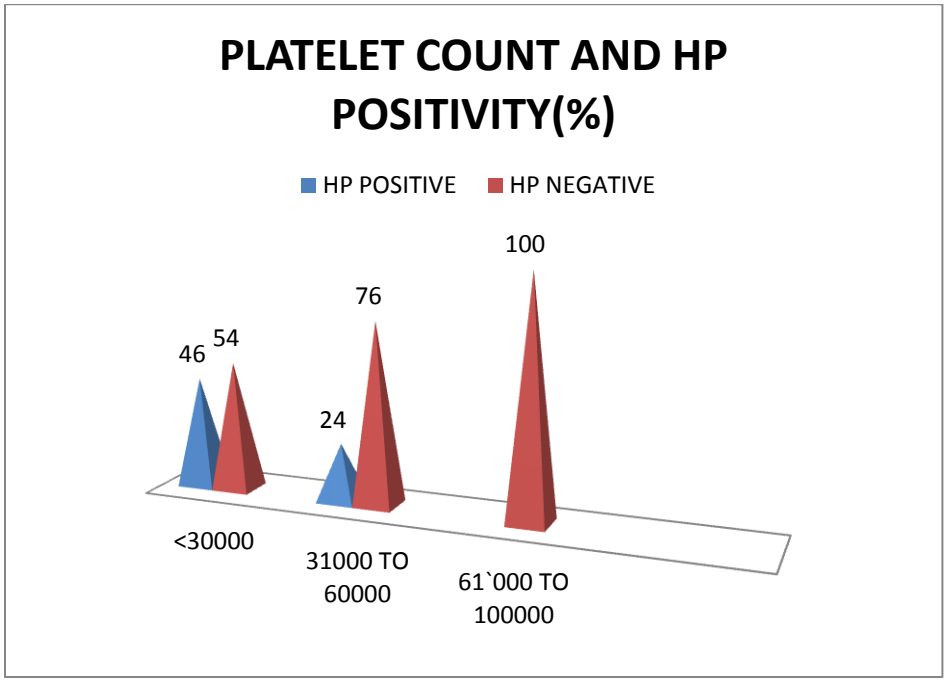
PLATELET COUNT AND ITP:

PLATELET COUNT	FREQUENCY	PERCENTAGE
<30000	30	60%
31000 TO 60000	17	34%
61000 TO 100000	3	6%



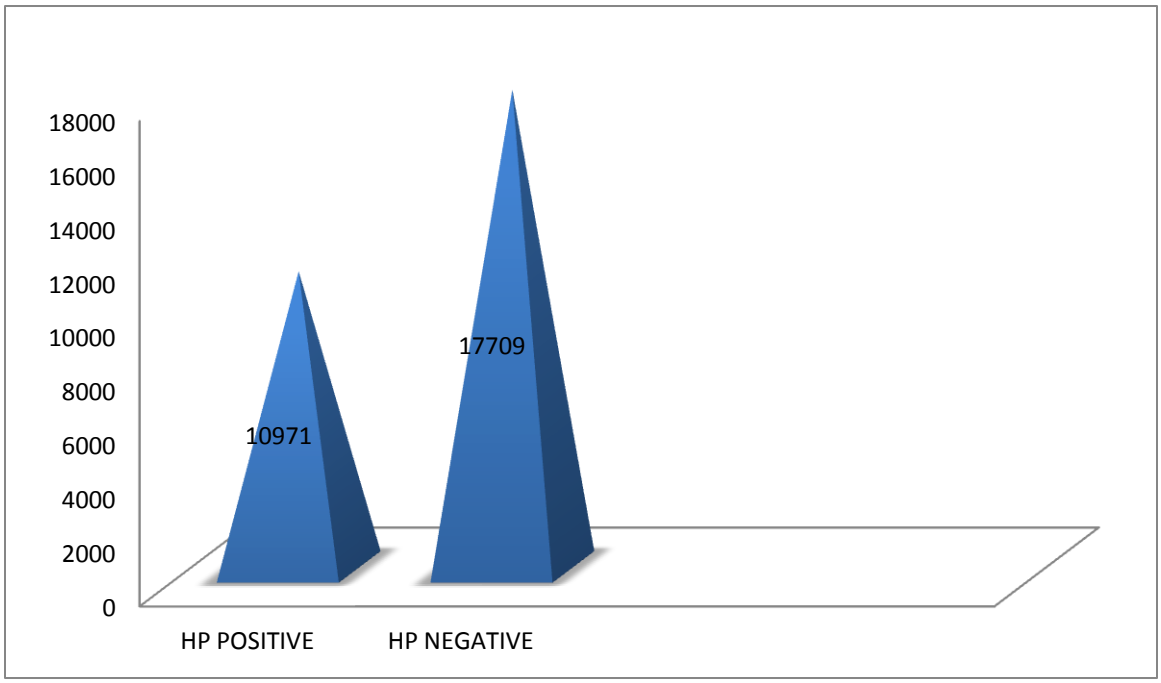
H.PYLORI POSITIVITY AND PLATELET COUNT:

PLATELET COUNT	HP POSITIVE	HP NEGATIVE
<30000	14(46%)	16(54%)
31000 TO 60000	4(24%)	13(76%)
60000 TO 100000	-	3(100%)



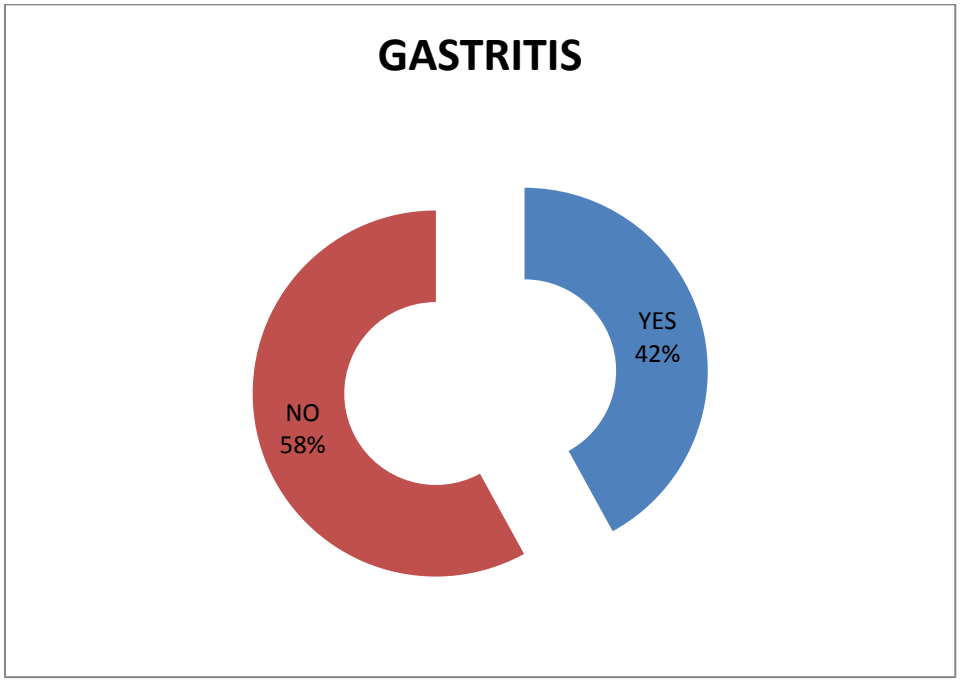
MEAN PLATELET COUNT IN H.PYLORI POSITIVE PATIENTS:

ITP	MEAN PLATELET COUNT
HP POSITIVE	10971.29
HP NEGATIVE	17709.80



ENDOSCOPY AND ITP:

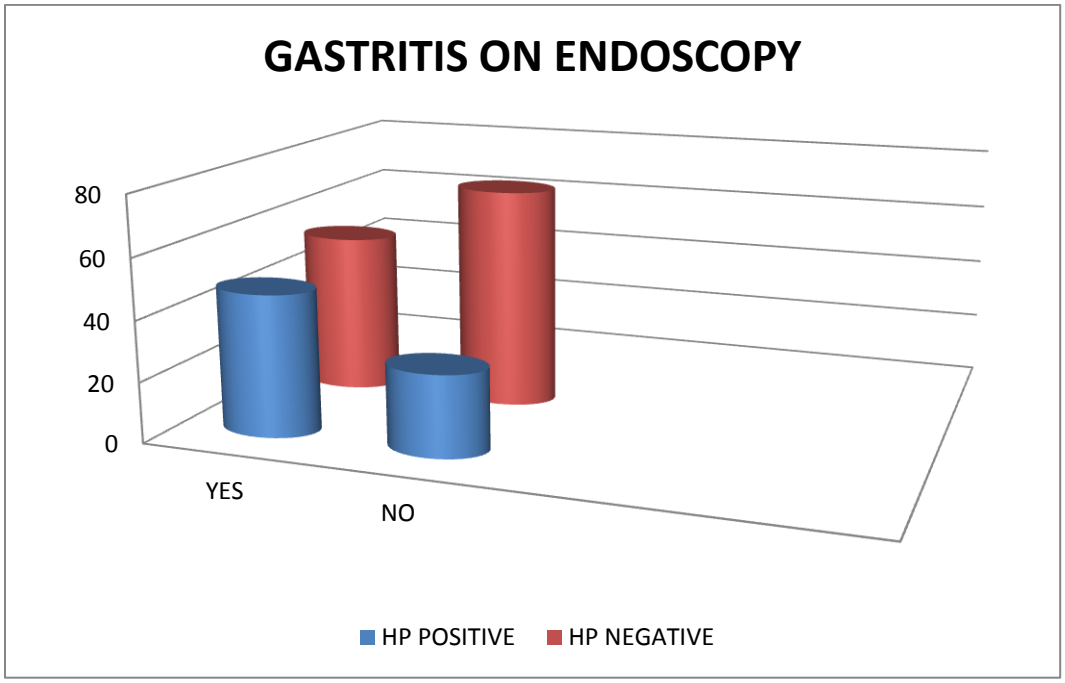
GASTRITIS	FREQUENCY	PERCENTAGE	MEAN PLATELET
PRESENT	21	42	26571.42
ABSENT	29	58	28793.10



ENDOSCOPY (GASTRITIS) AND H.PYLORI POSITIVITY:

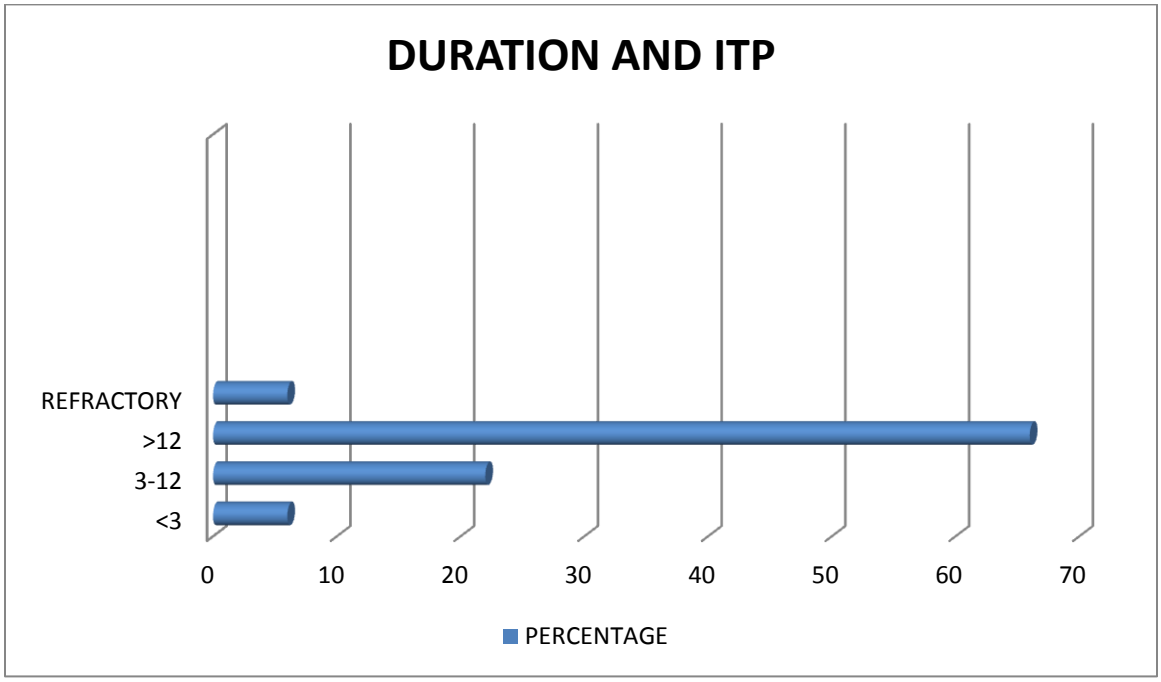
GASTRITIS	FREQUENCY	HP POSITIVE	HP NEGATIVE
YES	21	10(47%)	11(53%)
NO	29	8(27%)	21(73%)

P value is 0.23(not significant)



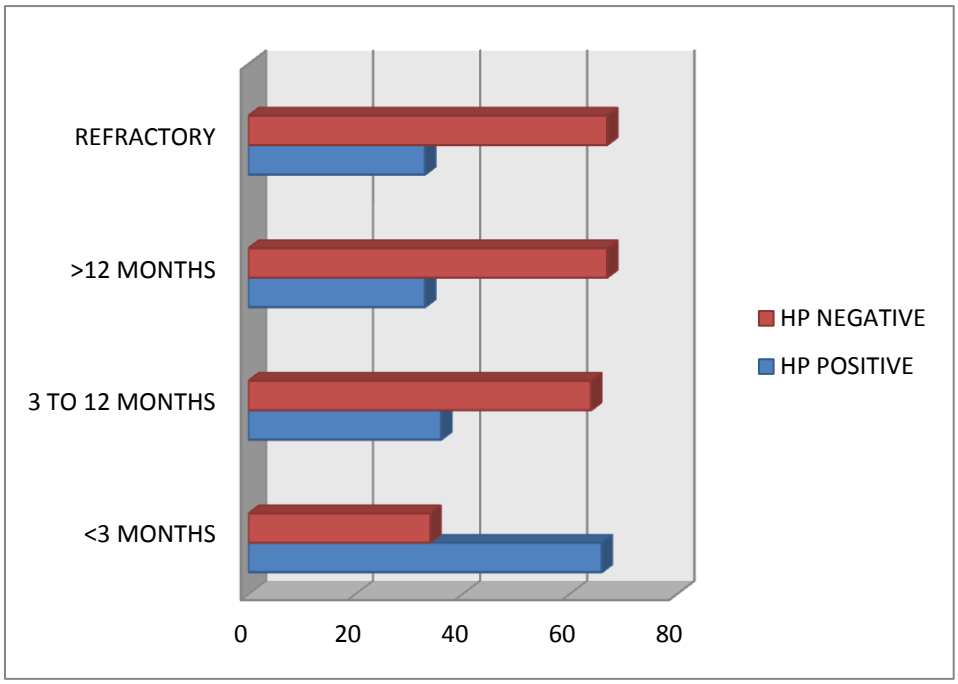
DURATION OF SYMPTOMS AND ITP:

DURATION	FREQUENCY	PERCENTAGE	MEAN PLATELET
<3 MONTHS	3	6	20000
3-12 MONTHS	11	22	29545
>12 MONTHS	33	66	28606
REFRACTORY	3	6	21333



DURATION OF SYMPTOMS AND H.PYLORI POSITIVITY:

DURATION	FREQUENCY	POSITIVE	NEGATIVE
< 3 MONTHS	3	2 (66.66%)	1 (33.33)
3 – 12 MONTHS	11	4 (36.36%)	7 (63.63)
> 12 MONTHS	33	11 (33.33%)	22 (66.66%)
REFRACTORY	3	1 (33.33%)	2 (66.66%)



MEAN PLATELET BASED ON DURATION AND HP POSITIVITY:

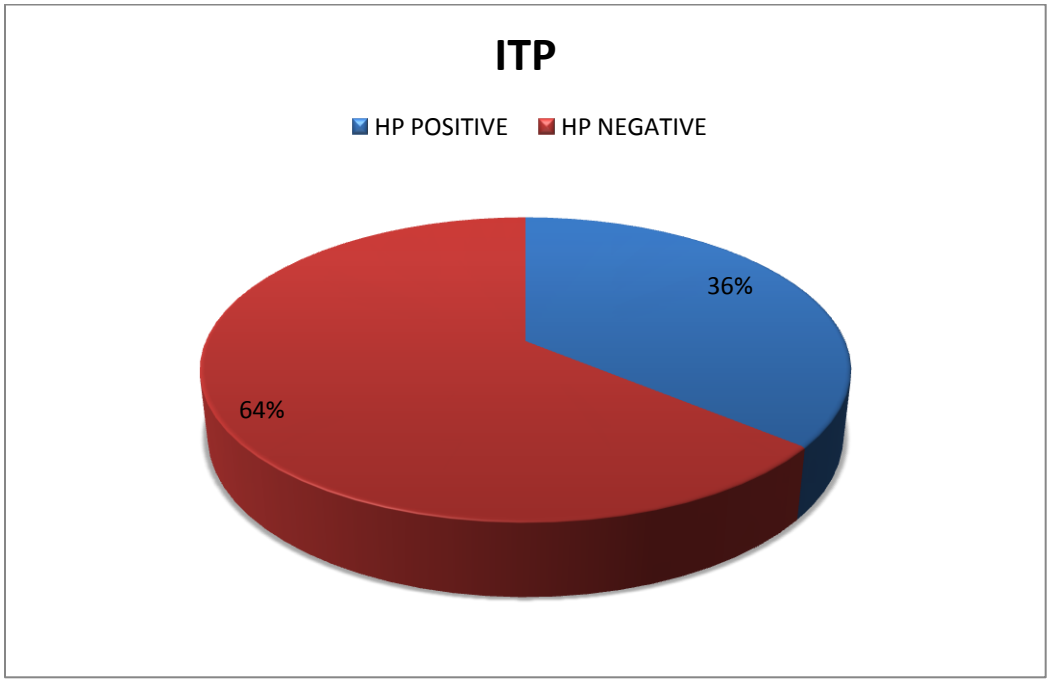
DURATION	HP POSITIVE	MEAN PLATELET
< 3MONTHS	2	12500
3 TO 12 MONTHS	4	11250
>12 MONTHS	11	23181
REFRACTORY	1	10000

MEAN PLATELET BASED ON DURATION AND HP NEGATIVITY:

DURATION	HP NEGATIVE	MEAN PLATELET
< 3 MONTHS	1	35000
3 TO 12 MONTHS	7	40000
>12 MONTHS	22	31318
REFRACTORY	2	27000

H.PYLORI POSITIVITY IN ITP:

ITP	FREQUENCY	PERCENTAGE
HP POSITIVE	18	36
HP NEGATIVE	32	64



RESULTS:

Our study was a cross sectional study in which we evaluated 50 patients with ITP. We analyzed their clinical profile and did an antral biopsy and subjected the specimen to rapid urease test, to detect the H.pylori status of the ITP patients.

SEX:

Out of the 50 patients 39 were female and 11 were male. The female: male ratio was 3.5:1. The frequency of H.pylori infection was equal among females (35.89%) and males (36%) although ITP was more common among females.

AGE:

Among the 50 patients 16 were in the third decade and 13 in the fourth decade and H.pylori positivity was also common in this age groups.

Mean age of ITP was 31.9 years (±12.42).

Mean age in males was 33.27 years and mean age in females was 31.5 years.

Mean age of H.pylori positive ITP patients was 32.4(±12.09) years and mean age of H.pylori negative ITP patients was 31.53(±29.0) years.

Mean age of H.pylori positive males (40±4.7 years) was higher than H.pylori positive females (30.28±12.79 years).

RESIDENCE:

In our study 38(76%) were from urban area and 12(24%) from rural area.

H.pylori positivity was more in rural population 41% (5 positive among 12) and it was 34% in urban area 34% (13 positive among 38).

Mean platelet in H.pylori positive individuals from urban and rural population was the same, It was 17,472.5 cells/cu.mm.

SOCIOECONOMIC STATUS:

Applying the Kuppusamy's criteria it was found that 84% (42 of 50) were from the lower class and 16% (8 of 50) from upper class. The frequency of H.pylori positivity was equal in both the upper class (37.5%) and lower class (35.7%).

CLINICAL PROFILE:

Bleeding: 88% (44 of 50) presented with bleeding and 12% (6 of 50) were asymptomatic. Among the patients with bleeding 50% had major bleed (GI bleed, genitor-urinary and intra cranial) and 50% presented with minor bleed(skin and mucous bleed).

H.pylori positivity was more frequent in patients with bleeding 38% (17 of 44 positive) than patients without bleeding 16% (1 of 6).

Mean platelet in ITP patients with bleeding and H.pylori positive was 17823 cells/cumm and H.pylori negative patients was 32148 cells/cumm.

Mean platelet in asymptomatic ITP patients and H.pylori positive was 32000 and H.pylori negative was 3800 cells /cumm.

Skin rash: 64% (32 of 50) of ITP patients had skin rash and H.pylori positivity was seen in 47% (15 positive of 32) of these patients. H.pylori positivity among patients without skin rash was only 16.6%.

Dyspepsia: Out of 50 patients only 13(26%) had dyspepsia and 74% had no dyspepsia. H.pylori positivity was only 7% among patients with dyspepsia as compared to 46% positivity in patients without dyspepsia.

PLATELET COUNT:

In our study 60% (30 of 50) had platelet counts less than 30000 and 34% (17 of 50) had platelet counts between 31000 and 60000 and6%(3 of 50) had platelet counts between 60000 and 100000. The mean platelet count of ITP patients was 27860(±17007.81) cells/cu mm.

All the 18 H.pylori positive patients had platelet counts less than 60,000, out of these 77%(14 of 18) had platelet <30000 and 23% (4 of 18) had platelet counts between 31000 and 60000. The mean platelet of H.pylori ITP patients was 10971(±10971.29)cells/cu mm and mean platelet of H.pylori negative ITP patients was 33062.5(±17709) cells/cu mm.

ENDOSCOPY (GASTRITIS):

Out of 50 patients 21 (42%) had gastritis on endoscopy and of these 47% (10 of 21) were positive for H.pylori. The remaining 29 (58%) did not have gastritis on endoscopy and of these only 27% (8 of 29) were H.pylori positive.

Out of 18 ITP patients positive for H.pylori 55% (10 patients) had gastritis on endoscopy.

The mean platelet count of H.pylori positive ITP patients with gastritis was 18100 and H.pylori negative ITP patients with gastritis was 34272 cells/cu mm.

The mean platelet of H.pylori positive patients without gastritis was 19250 and H.pylori negative patients without gastritis was 32,428 cells/cumm.

BLOOD GROUP:

In our study majority of the patients had O positive (54%) and B positive blood groups (22%).

14% were A positive, 4% AB positive , 4% B negative and 2% O negative respectively.

14 out of the 18 H.pylori positive patients were O positive. (77%).

DURATION OF ITP:

In our study 66% (33 of 50) had chronic ITP, 22% (11 of 50) had persistent ITP, 6% (3 of 50) had ITP of less than 3 months duration and 6% (3 of 50) had refractory ITP that is had spleenectomy done. The mean duration of ITP patients included in our study was 29.44(±25.331) months

61% (11 of 18) H.pylori positive ITP patients had chronic ITP,22% (4 of 18) had persistent.ITP 11% (2 of 18) had acute ITP and 6% (1 of 18) had refractory ITP.

H.pylori frequency was more among patients with acute ITP (66.66%) when compared to patients with persistent ITP (36.66%), chronic ITP (33.33%) and refractory ITP (33.33%).

The mean platelet of patients with H.pylori positive ITP was low (14232 cells/cumm) in all four groups compared to H.pylori negative ITP patients (333329 cells/cumm).

PREVALENCE OF H.PYLORI IN ITP:

Out of the 50 ITP patients 18 were H.pylori positive that is the prevalence was 36%. 32(64%) were H.pylori negative.

DISCUSSION:

CLINICAL CHARECTERISTICS OF H.PYLORI POSITIVE AND H.PYLORI NEGATIVE ITP PATIENTS:

CLINICAL FEATURES	H.PYLORI POSITIVE	H.PYLORI NEGATIVE	P VALUE	SIGNIFICANCE
SEX(M/F)	4/14	7/25	1	NS
RESIDENCE(U/R)	13/5	24/8	0.7	NS
SES(UC/LC)	3/15	5/27	1	NS
BLEEDING(Y/N)	17/1	27/5	0.3	NS
SKIN RASH(Y/N)	15/3	17/15	0.06	NS
DYSPEPSIA(Y/N)	1/17	12/20	0.32	NS
ENDOSCOPY (Y/) (GASTRITIS)	10/8	11/21	0.23	NS

P value <0.05 is considered statistically significant.

NS : Not significant

U/R : Urban/Rural, Y/N : Yes/No, M/F : Male/Female

SES : Socioeconomic Status, UC/LC : Upper class/Lower class.

Group Statistics for age, duration and platelet count:

	RUT	N	Mean	Std. Deviation	Std. Error Mean
Platelet count	Positive	18	18611.11	10971.293	2585.959
	Negative	32	33062.50	17709.005	3130.539
Duration	Positive	18	31.00	29.927	7.054
	Negative	32	28.56	22.823	4.035
AGE	Positive	18	32.44	12.099	2.852
	Negative	32	31.59	12.791	2.261

P values

Parameters	P value	Interpretation
Mean age	0.8	NS
Mean duration	0.76	NS
Mean platelet count	0.003	S

NS- not significant S-significant

CLINICAL CHARACTERISTICS:

AGE: Several studies have shown that ITP patients infected with H.pylori were found to be significantly older than ITP patients not infected with H.pylori.[8, 14] Prevalence of H.pylori increases with increasing age mostly seen in patients more than 30years.In our study mean age in H.pylori positive was 32.14 years and in H.pylori negative patients was 31.59 years and P value was 0.8 and hence was not statistically significant.

SEX: None of the studies demonstrated any difference in the prevalence of H.pylori infected males and females. The P value in our study was 1 and was not statistically significant.

DURATION: Duration of ITP is important in monitoring response to treatment of H.pylori. Shorter the duration better is the response.[8]The mean

duration of H.pylori positive patients was 31 months and H.pylori negative patients was 28.5 months. P value was 1 and was not significant.

DYSPEPSIA: Significant association between H.pylori positivity and dyspepsia was reported by Michel et al[16], but not by Stasi et al[8].In our study there was no significant association, P value was 0.38.

PLATELET COUNT: There were no studies which showed any significant association between the initial platelet count and H.pylori positivity.[8, 14] but most of the H.pylori infected ITP patients presented with severe form of ITP at the time of diagnosis In our study 14 of 18(77.77%) H.pylori ITP patients presented with severe ITP at the time of diagnosis and their platelet counts were <30000cells/cu mm and it is statistically significant, P value is 0.003.

Other parameters like residence, socioeconomic status, bleeding and presence of skin rashes were assessed, but were not clinically significant. The endoscopic finding of gastritis was also assessed in H.pylori positive and negative cases but was not significant

ASSOCIATION BETWEEN H.PYLORI AND ITP:

Recently H.pylori has been implicated in a number of autoimmune diseases like ITP.[11].The first association was proved in 1998 by Gasberrini et al[19].

Small study by Emilia et al[14] (13 positive of 30) also proved significant association.

In our study 18 (36%) were positive out 50 ITP patients. The P value was 0.048 and hence was statistically significant. So similar to other studies our study also proves significant association between H.pylori and ITP.

	Observed N	Expected N	Residual
Positive	18	25.0	-7.0
Negative	32	25.0	7.0
Total	50		

Test Statistics:

	RUT
CHI – SQUARE	3.920
Df	1
Asymp significance	0.048

Most of the studies in literature have found a high frequency of H.pylori infection in patients with ITP and it was observed that in most of them after the eradication of H.pylori there was a significant increase in platelet count.[12-15] World this association has been found in 27 other studies. A consolidated analysis of these studies shows that 65.7% of ITP patients are infected with H.pylori. In contrast some studies from USA[17] and France have reported only a low frequency of H.pylori infection .The possible explanation for this could be the low prevalence of H.pylori infection in this population. The reason for such discordant reports is uncertain but it might reflect the results of studying diverse patient groups, failure to stop concomitant treatment and the genetic diversity of H.pylori.

The frequency of H.pylori association with ITP reflected the prevalence of H.pylori in that geographical area. H.pylori positivity was propionate to the general population. This explains why most of the reports are from Japan and Italy .Successful H.pylori eradication led to good platelet response in areas where H.pylori infection rate in ITP patients was higher than in those where no association was found.[8]

LIMITATIONS:

1. Long term follow up not done.

2. H.pylori positive patients were treated but their platelet response was not monitored.

3. Results need to be confirmed in a larger group of patients and longitudinal groups.

CONCLUSION:

- The present study confirms the existence of association between H.pylori and ITP ($P < 0.05$).
- Our study also showed a significant association between the platelet counts at presentation in H.pylori positive ITP patients.
- There was no significant association with other parameters like sex, age, residence, socioeconomic status, bleeding, dyspepsia and endoscopy findings.
- Considering the low costs and non-invasiveness of the diagnostic test and the favorable toxicity profile of eradication compared to the standard treatment for ITP the detection and eradication of H.pylori should be considered in high prevalent areas. The British society of Hematology recommends H.pylori eradication and screening as a treatment in ITP.

BIBLIOGRAPHY:

.1. Harrison's principles of Internal Medicine 18th edition.

2 .Cines DB, Bussel JB, Liebman HA, Luning Prak ET. The ITP syndrome: pathogenic and clinical diversity. *Blood*. 2009;113:6511–6521.

3. Francesco Rodeghiero, Roberto STASI, Terry Gernsheimer, Marc Michel. Standardisation of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. Blood, 12 march 2009 volume113, 11 : 2386-2393.

4. Adam Cuker and Douglas B.Cines. Immune Thrombocytpenia American Society of Hematology. Hematology 2010 377 -384.

5. Provan D, Stasi R, Newland AC, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. *Blood.* 2010;115:168 –186.

6.University of Michigan Pediatric Heme/Onc Program.

7. Kashif Hafeez Shaikh, Suhaib Ahmed, Muhhamud Ayub. Association of Helicobacter pylori infection with Idiopathic Thrombocytopenic Purpura. J Pak Med Assoc, October 2009 vol 59, no. 10, 661-663.

8. Emilia G, Luppi M, Zucchini P, et al. Helicobacter pylori infection and chronic immune thrombocytopenic purpura: long-term results of bacterium eradication and association

with bacterium virulence profiles. Blood. 2007;110:3833-3841.

9. Douglas B.Cines ITP: time to "bug off" Blood December 2007 volume 110, no.12, 3818 -3819

10. Kandulski A, Selgrad M, Malfertheiner P. Helicobacter pylori infection: a clinical overview. Dig Liver Dis 2008; 40: 619-26.

11. Prelipcean CC, Mihai C, Gogalniceanu P, Mitrica D, Drug VL, Stanciu C. Extragastric manifestations of Helicobacter pylori infection. Rev Med Chir Soc Med Nat Iasi 2007; 111: 575-83.

12. Gasbarrini A, Franceschi F, Tartaglione R, Landolfi R, Pola P, Gasbarrini G. Regression of autoimmune thrombocytopenia after eradication of Helicobacter pylori. Lancet 1998; 352:878.

13. Campuzano-Maya G. Proof of an association between Helicobacter pylori and idiopathic thrombocytopenic purpura in Latin America. Helicobacter 2007; 12: 265-73.

14. Emilia G, Luppi M, Zucchini P, Morselli M, Potenza L, Forghieri F, et al. Helicobacter pylori infection and chronic immune thrombocytopenic

purpura: long-term results of bacterium eradication and association with bacterium virulence profiles. Blood 2007; 110: 3833-41.

15. Rostami N, Keshtkar-Jahromi M, Rahnavardi M, Esfahani FS. Effect of eradication of Helicobacter pylori on platelet recovery in patients with chronic idiopathic thrombocytopenic purpura: a controlled trial. Am J Hematol 2008; 83: 376-81.

16. Michel M, Cooper N, Jean C, Frissora C, Bussel JB. Does Helicobacter pylori initiate or perpetuate immune thrombocytopenic purpura? Blood 2004; 103: 890-6.

17. Stasi.R, Ameet Sarpatwari, Jodi B. Segal. Effects of eradication of Helicobacter pylori infection in patients with immune thrombocytopenic purpura: a systematic review. Blood, 5 feb 2009, volume 113, 6: 1231-1240.

18. Suerbaum S, Michetti P. *Helicobacter pylori* infection. N Engl J Med. 2002;347:1175-1186.

19. Gasbarrini A, Franceschi F. Autoimmune diseases and *Helicobacter pylori* infection. Biom Pharmacother. 1999;53:223-226.

20. Gasbarrini A, Franceschi F, Tartaglione R, Landolfi R, Pola P, Gasbarrini G. Regression of autoimmune thrombocytopenia after eradication of*Helicobacter pylori*. Lancet. 1998;352:878.

21. Emilia G, Longo G, Luppi M, et al. *Helicobacter pylori* eradication can induce platelet recovery in idiopathic thrombocytopenic purpura. Blood. 2001;97:812-814.

22. Emilia G, Luppi M, Morselli M, Potenza L, D'Apollo N, Torelli G. *Helicobacter pylori* infection and idiopathic thrombocytopenic purpura. Br J Haematol. 2002;118:1198-1199.

23. Kohda K, Kuga T, Kogawa K, et al. Effect of *Helicobacter pylori* eradication on platelet recovery in Japanese patients with chronic idiopathic thrombocytopenic purpura and secondary autoimmune thrombocytopenic purpura. Br J Haematol. 2002; 118:584-588.

24. Veneri D, Franchini M, Gottardi M, et al. Efficacy of *Helicobacter pylori* eradication in raising platelet count in adult patients with idiopathic thrombocytopenic purpura. Haematologica. 2002;87: 1177-1179.

25. Hino M, Yamane T, Park K, et al. Platelet recovery after eradication of *Helicobacter pylori* in patients with idiopathic thrombocytopenic purpura. Ann Hematol. 2003;82:30-32.

26. Ando K, Shimamoto T, Tauchi T, et al. Can eradication therapy for *Helicobacter pylori* really improve the thrombocytopenia in idiopathic thrombocytopenic purpura? Our experience and a literature review. Int J Hematol. 2003;77:239-244.

27. Stasi R, Rossi Z, Stipa E, Amadori S, Newland AC, Provan D. *Helicobacter pylori* eradication in the management of patients with idiopathic thrombocytopenic purpura. Am J Med. 2005;118: 414-419.

28. Inaba T, Mizuno M, Take S, et al. Eradication of *Helicobacter pylori* increases platelet count in patients with idiopathic thrombocytopenic purpura in Japan. Eur J Clin Invest. 2005;35:214-219.

29. Fujimura K, Kuwana M, Kurata Y, et al. Is eradicatiotherapy useful as first line treatment in *Helicobacter pylori*-positive idiopathic thrombocytopenic purpura? Analysis of 207 eradicated chronic ITP cases in Japan. Int J Hematol. 2005; 81:162-168.

30. Suzuki T, Matsushima M, Masui A, et al. Effect of *Helicobacter pylori* eradication in patients with chronic idiopathic thrombocytopenic purpura: a randomized controlled trial. Am J Gastroenterol. 2005;100:1265-1270.

31. Veneri D, Krampera M, Franchini M. High prevalence of sustained remission of idiopathic thrombocytopenic purpura after *Helicobacter pylori* eradication: a long-term follow-up study. Platelets. 2005;16:117-119.

32. Suvajdzic N, Stankovic B, Artiko V, et al. *Helicobacter pylori* eradication can induce platelet recovery in chronic idiopathic thrombocytopenic purpura. Platelets. 2006;17:227-230.

33. Sayan O, Akyol E, Ozturk A. The efficacy of *Helicobacter pylori* eradication in the treatment of idiopathic thrombocytopenic purpura: the first study in Turkey. Acta Haematol. 2006;116:146-149.

34. Campuzano-Maya G. Proof of an association between *Helicobacter pylori* and idiopathic thrombocytopenic purpura in Latin America. Helicobacter. 2007;12:265-273.

35. Emilia G, Luppi M, Torelli G. Infectious agents and human immune diseases: lessons from *Helicobacter pylori.* Am J Med. 2005;118:420-421.

36. George JN, Woolf SH, Raskob GE, et al. Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. Blood. 1996;88: 3-40.

37. Tummuru MKR, Cover TL, Blaser MJ. Cloning and expression of a high-molecular-mass major antigen of *Helicobacter pylori*: evidence of linkage to cytotoxin production. Infect Immun. 1993;61:1799-1809.

38. Atherton JC, Cao P, Peck RM Jr, et al. Mosaicism in vacuolating cytotoxin alleles of *Helicobacter pylori*: association of specific vacA types with cytotoxin production and peptic ulceration. J Biol Chem. 1995;270:17771-17777.

39. Rudi J, Rudy A, Maiwald M, et al. Direct determination of *Helicobacter pylori* vacA genotypes and *cagA* gene in gastric biopsies and relationship to gastrointestinal diseases. Am J Gastroenterol. 1999;94:1525-1531.

40. van Doorn LJ, Figueiredo C, Sanna R, et al. Clinical relevance of the *cagA*, vacA, and iceA status of *Helicobacter pylori*. Gastroenterology. 1998; 115:58-66.

41. Gerhard M, Lehn N, Neumayer N, et al. Clinical relevance of the *Helicobacter pylori* gene for blood-group antigen-binding adhesin. Proc Natl Acad Sci U S A. 1999;96:12778-12783.

42. Ando T, Tsuzuki T, Mizuno T, et al. Characteristics of *Helicobacter pylori*-induced gastritis and the effect of *H. pylori* eradication in patients with chronic idiopathic thrombocytopenic purpura. Helicobacter. 2004;9:443-452..

ANNEXURES:

INSTITUTE OF INTERNAL MEDICINE

MMC & RGGGH, CHENNAI-3

PROFOMA

NAME : ADDRESS :

AGE/SEX :

OCCUPATION : PHONE NO.

COMPLAINTS :

EASY FATIGUEABILITY : Y/N

BLEEDING MANIFESTATIONS : GUMS/HEMATURIA/EPISTAXIS

BRUISING AT INJECTION SITE: Y/N

BONE PAIN : Y/N

FEVER : Y/N

SKIN RASHES : Y/N

JOINT PAIN : Y/N

DRUG INTAKE : Y/N

PAST HISTORY

DM : CAD:

SHT : STROKE/TIA:

CKD : CCF:

FAMILY H/O BLEEDING DISORDERS: Y/N

PERSONAL HISTORY

Smoker :

Alcoholic :

GENERAL EXAMINATION

BP : PULSE :

WEIGHT : HEIGHT :

PETECHIAE:

ECCHYMOSIS:

BLEEDING SPOTS IN THE BUCCAL MUCOSA:

SYSTEMIC EXAMINATION :

CVS:

RS:

P/A:

CNS:

INVESTIGATIONS :

CBC:

DATE					
HB					
TC					
DC					
ESR					
PLATELET					

MCV: MCH: MCHC:

PERIPHERAL SMEAR:

PT: APTT: INR:

BLOOD GROUP:

LDH: RETIC COUNT:

USG ABDOMEN:

ANA:

BONE MARROW ASPIRATION:

HBsAg:

ANTI-HCV:

HIV 1 AND 2:

ENDOSCOPIC BIOPSY AND RAPID UREASE TEST:

SERIAL NO	AGE	SEX	OCCUPATION	SOCIO ECONOMIC STATUS	RESIDENCE	BLEEDING	SKIN RASH	DYSPEPSIA	PLATELET COUNT	ENDOSCOPY FINDING	RAPID UREASE TEST	BLOOD GROUP	DURATION
1	41	F	HW	LC	URBAN	YES(G)	YES	YES	50,000	POSITIVE(AG)	NEGATIVE	O positive	15
2	16	F	STUDENT	LC	URBAN	YES(G)	YES	NO	10,000	POSITIVE(AG)	NEGATIVE	B POSITIVE	48
3	21	F	HW	LC	URBAN	YES(G,E)	YES	NO	30,000	NEGATIVE	NEGATIVE	O positive	5
4	26	F	HW	LC	URBAN	YES(G,E)	NO	NO	31,000	NEGATIVE	POSITIVE	B POSITIVE	60
5	17	M	L	UC	RURAL	YES(G,E)	NO	YES	20,000	NEGATIVE	NEGATIVE	O positive	30
6	18	F	STUDENT	LC	URBAN	YES(G)	NO	YES	15,000	NEGATIVE	NEGATIVE	A POSITIVE	28
7	40	F	L	LC	RURAL	YES(M)	YES	NO	20,000	NEGATIVE	POSITIVE	O positive	72
8	35	F	HW	LC	URBAN	YES(G,H,E)	YES	NO	10,000	NEGATIVE	NEGATIVE	O positive	18
9	16	F	STUDENT	LC	URBAN	YES(G)	NO	YES	30,000	NEGATIVE	NEGATIVE	B POSITIVE	49
10	60	F	HW	LC	URBAN	YES(PR)	YES	NO	22,000	POSITIVE(AG)	NEGATIVE	O positive	18
11	35	M	AD	UC	URBAN	YES(G)	YES	NO	20,000	POSITIVE(AG)	POSITIVE	O positive	1
12	40	F	HW	LC	URBAN	YES(M)	YES	NO	15,000	NEGATIVE	NEGATIVE	B POSITIVE	5
13	30	f	HW	LC	URBAN	YES(G,H,E,M)	YES	NO	10,000	NEGATIVE	POSITIVE	O positive	8
14	58	F	HW	LC	URBAN	YES(M)	NO	NO	30,000	NEGATIVE	NEGATIVE	O positive	10
15	42	M	FARMER	LC	RURAL	YES(PR)	NO	NO	52000	POSITIVE(PG)	NEGATIVE	B POSITIVE	12
16	20	F	L	LC	RURAL	YES(G,M)	YES	NO	20,000	POSITIVE(AG)	NEGATIVE	O positive	13
17	21	F	L	UC	URBAN	YES(G)	YES	NO	64000	NEGATIVE	NEGATIVE	O positive	36
18	43	M	L	LC	URBAN	NO	NO	NO	32000	POSITIVE(AG)	POSITIVE	A POSITIVE	17
19	25	F	HW	LC	URBAN	YES(G,H,E)	YES	NO	10000	POSITIVE(PG)	POSITIVE	O positive	108
20	24	F	HW	UC	URBAN	NO	NO	YES	45000	NEGATIVE	NEGATIVE	B POSITIVE	22
21	12	F	STUDENT	UC	URBAN	YES(G)	YES	NO	45000	POSITIVE(PG)	POSITIVE	O positive	16
22	29	M	L	LC	URBAN	YES(G,H,E)	YES	YES	10000	POSITIVE(PG)	NEGATIVE	O positive	28
23	25	F	HW	UC	URBAN	NO	NO	NO	34000	NEGATIVE	NEGATIVE	B POSITIVE	88
24	45	M	L	LC	URBAN	YES(E)	YES	NO	20000	POSITIVE(AG)	POSITIVE	O positive	34
25	50	F	HW	LC	RURAL	YES(G)	NO	NO	36000	NEGATIVE	NEGATIVE	A POSITIVE	38
26	18	F	L	LC	URBAN	NO	YES	NO	37000	NEGATIVE	NEGATIVE	A POSITIVE	17
27	56	F	HW	LC	URBAN	YES(G)	NO	NO	40000	NEGATIVE	NEGATIVE	O positive	18
28	37	M	L	LC	URBAN	YES(G,E)	YES	NO	20000	NEGATIVE	POSITIVE	O positive	34
29	30	F	HW	LC	RURAL	YES(G,E,M)	YES	NO	5000	POSITIVE(PG)	POSITIVE	O positive	2
30	35	F	HW	LC	URBAN	YES(G,E)	NO	NO	20000	NEGATIVE	NEGATIVE	AB POSITIVE	40
31	50	F	HW	LC	URBAN	YES(G)	YES	NO	32000	NEGATIVE	POSITIVE	O positive	72
32	21	F	HW	LC	RURAL	YES(G,M)	YES	YES	21000	NEGATIVE	POSITIVE	O NEGATIVE	6
33	34	F	HW	LC	RURAL	YES(G)	YES	NO	32000	NEGATIVE	NEGATIVE	A POSITIVE	75
34	30	F	HW	LC	URBAN	YES(G)	YES	NO	15000	POSITIVE(PG)	POSITIVE	O POSITIVE	42
35	60	F	HW	LC	URBAN	YES(G)	NO	NO	20000	POSITIVE(PG)	POSITIVE	B NEGATIVE	17
36	22	F	HW	LC	URBAN	NO	NO	YES	62000	POSITIVE(AG)	NEGATIVE	B POSITIVE	45
37	24	F	TEACHER	UC	URBAN	YES(G,M)	YES	NO	5000	NEGATIVE	POSITIVE	O POSITIVE	39
38	17	F	STUDENT	LC	RURAL	YES(M)	NO	NO	60000	POSITIVE(AG)	NEGATIVE	A POSITIVE	15
39	31	M	L	LC	URBAN	NO	YES	NO	12000	POSITIVE(AG)	NEGATIVE	A POSITIVE	29
40	48	F	HW	LC	URBAN	YES(G,M)	YES	NO	64000	NEGATIVE	NEGATIVE	AB POSITIVE	60
41	31	F	HW	LC	URBAN	YES(G,M)	YES	YES	20000	NEGATIVE	NEGATIVE	B NEGATIVE	85
42	37	F	HW	LC	URBAN	YES(G,E)	YES	NO	35000	POSITIVE(PG)	NEGATIVE	O positive	3
43	27	M	L	LC	URBAN	YES(G,H)	YES	NO	10000	NEGATIVE	NEGATIVE	o positive	23

SERIAL NO	AGE	SEX	OCCUPATION	SOCIO ECONOMIC STATUS	RESIDENCE	BLEEDING	SKIN RASH	DYSPEPSIA	PLATELET COUNT	ENDOSCOPY FINDING	RAPID UREASE TEST	BLOOD GROUP	DURATION
44	16	F	STUDENT	LC	URBAN	YES(M)	YES	YES	5000	POSITIVE(AG)	POSITIVE	O positive	12
45	40	F	HW	UC	URBAN	YES(G,E,M)	YES	YES	20000	NEGATIVE	NEGATIVE	B POSITIVE	16
46	28	M	L	LC	RURAL	YES(G)	NO	NO	47000	NEGATIVE	NEGATIVE	B POSITIVE	6
47	35	F	HW	LC	RURAL	YES(G,E,M)	YES	NO	15000	NEGATIVE	POSITIVE	O positive	14
48	22	F	HW	LC	URBAN	YES(M)	NO	NO	62000	NEGATIVE	NEGATIVE	B POSITIVE	12
49	32	M	L	LC	URBAN	YES(E)	NO	YES	44000	POSITIVE(PG)	NEGATIVE	O positive	7
50	25	F	HW	LC	RURAL	YES(E,M)	YES	YES	9000	POSITIVE(AG)	POSITIVE	O positive	4

KEYWORDS

M	MALE
F	FEMALE
HW	HOUSE WIFE
L	LABOURER
AD	ADVOCATE
LC	LOWER CLASS
UC	UPPER CLASS
G	GUM BLEED
E	EPISTAXIS
M	MENORRHAGIA
H	HEMATURIA

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. Anny Antony
PG in MD General Medicine
Madras Medical College, Chennai -3

Dear Dr. Anny Antony

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "Immune thrombocytopenic purpura and its association with helicobacter pylori infection" No.31042012.

The following members of Ethics Committee were present in the meeting held on 19.04.2012 conducted at Madras Medical College, Chennai -3.

1.	Dr. S.K. Rajan. M.D.,FRCP.,DSc	-- Chairperson
2.	Prof. Pregna B. Dolia MD Director , Institute of Biochemistry, MMC, Ch-3	-- Member Secretary
3.	Prof. B. Kalaiselvi MD Prof. of Pharmacology ,MMC, Ch-3	-- Member
4.	Prof. C. Rajendiran, MD Director , Inst. of Internal Medicine, MMC, Ch-3	-- Member
5.	Prof. Md. Ali. MD.DM Prof & HOD, Dept. of MGE, MMC, Ch-3	-- Member
6.	Prof.P.Karkuzhali MD Director i/c, Prof., Inst. of Pathology, MMC, Ch-3	-- Member
7.	Prof. S. Deivanayagam MS Prof of Surgery, MMC, Ch-3	-- Member
8.	Prof. A. Radhakrishnan MD Prof of Internal Medicine, MMC, Ch-3	-- Member
9.	Thiru. S. Govindsamy. BABL	-- Lawyer
10.	Tmt. Arnold Soulina MA MSW	-- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

turnitin

Your digital receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

Paper ID	293748995
Paper title	IMMUNE THROMBOCYTOPENIC PURPURA AND ITS ASSOCIATION WITH HELICOBACTER PYLORI INFECTION
Assignment title	Medical
Author	Anny Antomy 20101002 M.D. General Medicine
E-mail	md.anny.85@gmail.com
Submission time	21-Dec-2012 09:14PM
Total words	9549

First 100 words of your submission

DISSERTATION TITLED “IMMUNE THROMBOCYTOPENIC PURPURA AND ITS ASSOCIATION WITH HELICOBACTER PYLORI INFECTION” Submitted in partial fulfilment of Requirements for M.D.DEGREE EXAMINATION BRANCH-I INTERNAL MEDICINE THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY CHENNAI INSTITUTE OF INTERNAL MEDICINE MADRAS MEDICAL COLLEGE CHENNAI - 600003. APRIL-2013 CERTIFICATE This is to certify that the dissertation entitled “IMMUNE THROMBOCYTOPENIC PURPURA AND ITS ASSOCIATION WITH HELICOBACTER PYLORI INFECTION”is a bonafide work done by DR.ANNY ANTONY , Post Graduate Student, Institute of Internal Medicine, Madras Medical College, Chennai-3, in partial fulfillment of the University Rules and Regulations for the...